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The scientific background of the International Sanitary Conferences 1851-1938

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CONTENTS

	Page
Preface	7
Introduction	9
The first conference: Paris, 1851	12
The second conference: Paris, 1859	17
The third conference: Constantinople, 1866	23
The fourth conference: Vienna, 1874	35
The fifth conference: Washington, 1881	42
The sixth conference: Rome, 1885	46
The seventh conference: Venice, 1892	58
The eighth conference: Dresden, 1893	66
The ninth conference: Paris, 1894	71
The tenth conference: Venice, 1897	78
The eleventh conference: Paris, 1903	81
The founding of the Office international d'Hygiène publique, 1907	86
The twelfth conference: Paris, 1911-1912	89
The thirteenth and fourteenth conferences: Paris, 1926 and 1938	93
Conclusion	99
Bibliographical notes	101
Index	105

ILLUSTRATIONS

	Page
The facies in cholera, Vienna, 1831	10
Europe in 1851	13
<i>Berliner Cholera-Zeitung</i> , 1831	14
Treatment of cholera by heat, 1831	16
Cholera in Paris, 1832	18
"A Court for King Cholera", 1852	19
Michael Faraday and Father Thames, 1855	21
Proceedings of the third Conference, Constantinople, 1866	24
Clot's "proof" of the non-contagiousness of plague, 1835	26
Filippo Pacini (1812-1883)	28
William Farr (1807-1883)	29
August Hirsch (1817-1892)	33
Max von Pettenkofer (1818-1901)	36
Opening of the Suez Canal, 1869	41
Carlos Finlay (1833-1915)	44
Robert Koch (1843-1910)	48
Sir Joseph Fayrer (1824-1907)	53
Sir John Burdon-Sanderson (1828-1905)	59
Sir Charles Sherrington (1857-1952)	60
<i>Zum gegenwärtigen Stand der Cholerafrage</i>	62
The first International Sanitary Convention to come into force	65
Heat sterilization of faeces, St Petersburg, 1892	67
The Ka'ba, Mecca	72
The El Tor quarantine station, 1892	73
Alexandre Yersin (1863-1943)	79
Albert Calmette (1863-1933) and Camille Guérin (1863-1933)	80
Ion Cantacuzino (1863-1934)	81
Adrien Proust (1834-1903)	82
Emile Roux (1853-1933)	83
William Crawford Gorgas (1854-1920)	84
Coffins of plague victims at Harbin, 1911	94
Hideyo Noguchi (1876-1928)	97
Adrian Stokes (1887-1927)	98
The first and last International Sanitary Conferences	99

PREFACE

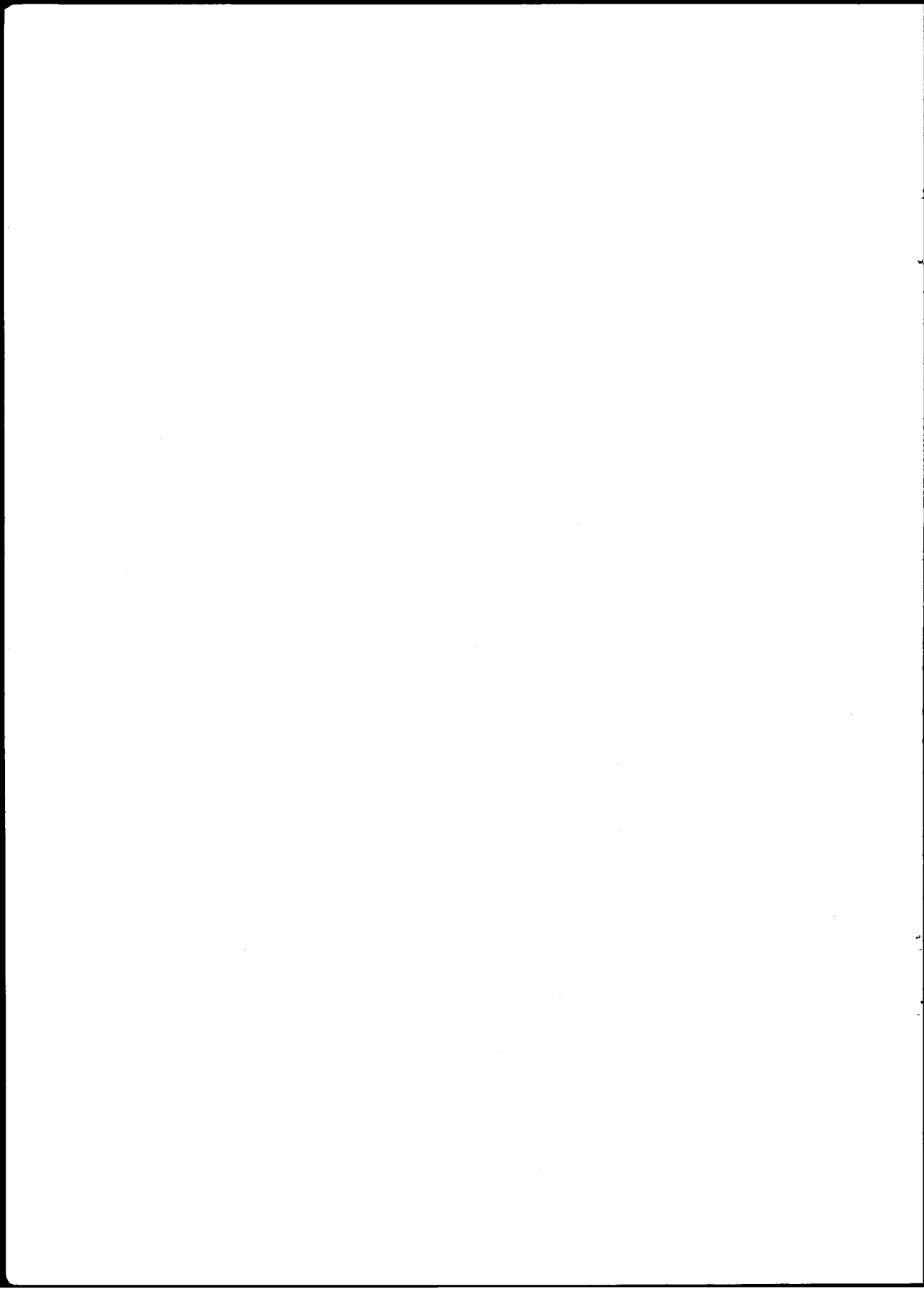
It is almost thirty years since the nations decided that the World Health Organization should be founded as the single agency for directing and coordinating intergovernmental health activities. Subsequent developments have been very fully documented in two WHO publications respectively on the first and second decades of the Organization's existence and in the series of annual reports that started in 1948. But WHO did not come into being as a result of some process of spontaneous generation. As it exists today, it represents the culmination of over 120 years of strivings, at first with very limited objectives, towards intergovernmental cooperation in understanding and solving health problems. For the first four decades, international agreement was frustrated by lack of scientific knowledge. Since then, every gain to knowledge won by medical research has increased the possibilities of fruitful international cooperation for the benefit of all mankind.

In 1943 Sir Edward Mellanby wrote:

"The work of Government Departments. . . of medical men . . ., and of nursing staff in controlling disease can only be as good as knowledge allows it to be, and this knowledge has come, and can only come by medical research."

There is no more striking demonstration of Mellanby's assertion than that provided by the early history of international health cooperation, for which medical research provided the missing link. In the future, every advance made by medical research will facilitate the broadening of the scope of WHO's activities.

The present study is largely based on work done during the tenure in 1971-72 of an appointment as visiting scientist, National Library of Medicine, National Institutes of Health, Public Health Service, Department of Health, Education and Welfare, USA. The author wishes to acknowledge his indebtedness to Dr Martin M. Cummings, Director of the National Library of Medicine, and Dr John B. Blake, Chief of its History of Medicine Division, for having facilitated access to the superb historical resources of this great library.



Introduction

About two centuries ago Samuel Johnson, the English philosopher, wit, and lexicographer, said: "Whatever makes the past, the distant, or the future, predominate over the present, advances us in the dignity of thinking beings." But, beyond this, a study of the historical evolution of present scientific ideas and institutions helps to place them in perspective, to measure the progress made, and, by extrapolation, to predict future trends.

While it was not until 1948 that the World Health Organization came into being, it represents the culmination of efforts at international health cooperation that started almost a century before when the first International Sanitary Conference opened in Paris on 23 July 1851. Ten such conferences took place during the nineteenth century, and the seventh of them was the first to produce any tangible result. Nevertheless, these conferences provided a unique forum for the international exchange of ideas between medical administrators and medical scientists of different nations and cultures. Their printed proceedings are of extraordinary scarcity, as only a few copies were issued for distribution to participating governments. Two libraries—the library of the World Health Organization and the National Library of Medicine, Bethesda, Md.—are probably the only ones in the world with the complete series, either in the form of originals or photocopies. And the completion of the holdings of these two libraries was achieved as late as 1971 by the mutual exchange of duplicates and photocopies.

That these printed records should be so inaccessible is to be regretted, for they constitute a living history of the different conceptions of the nature of epidemic diseases held during the latter half of the nineteenth century and immediately after. The discussions at these international confrontations vividly reflect medical thinking as it really was, and provide a salutary corrective to the foreshortened and romanticized accounts of individual discoveries that often pass for medical history. They also show very clearly that all hopes of international agreement on preventive measures against epidemic diseases were illusory as long as the partisan conflict between rival hypotheses did duty for scientific

proof of their real etiology and epidemiology. For some four decades these conferences produced no result, and it says much for the early pioneers of international health cooperation that they had the tenacity to pursue their deliberations. But as the etiologies of cholera, then plague, and then yellow fever were unravelled, the pace of international health cooperation quickened, leading to the foundation, one after the other, of the Pan American Sanitary Bureau, the Office international d'Hygiène publique, the Health Organisation of the League of Nations, and, finally, the World Health Organization, which incorporated all its predecessors.

The records of the International Sanitary Conferences show not only how long and uphill was the road that eventually led to WHO but also how scientific knowledge that has been painfully won may be forgotten and, decades later, rediscovered. Thus, in the 1960s the concepts of convalescent cholera carriers, of mild or inapparent infections, and of the gall bladder as a reservoir of cholera vibrios were trumpeted as new discoveries. Yet the records show that all these concepts were universally accepted some sixty or more years ago. That they faded into oblivion for so long is doubtless because cholera had been unknown for many years in the countries where medical research and teaching were most advanced. The increase in the amount and speed of air travel has changed all that, and public health authorities in all countries must now be alert to the possibility that arriving passengers, often returning tourists, may be harbouring the disease.

During the nineteenth century, cholera was the main or the sole subject of discussion at most of the International Sanitary Conferences. It was the disease that, more than all others combined, stimulated the nations to persist in their efforts to reach agreement on the measures to be taken to limit the spread of epidemic diseases.

The background to the first of the International Sanitary Conferences may be briefly sketched as follows. Asiatic cholera first reached the fringes of Europe when it broke out in 1829 at Orenburg, at the south-eastern extremity of the Russian Empire, having slowly travelled overland from India via the



*Jeune femme de Vienne?
âgée de 23 ans.*



*La même, 1 heure après l'invasion du Choléra,
et ¼ d'heure avant sa mort.*

WHO photograph from original
in the author's possession

Cholera made its European début in Russia and rapidly spread to Poland and then to Austria. Other European countries that were as yet unaffected sent governmental medical missions to investigate and report on this frightening new pestilence. Among these was a two-man mission sent by the Royal Academy of Medicine of Paris in June 1831 on behalf of the French Government to Russia, Prussia, and Austria, the members of which were Auguste Gerardin and Paul Gaimard.¹ On their way to St Petersburg they stopped for a few hours at Weimar, where they had the "signal honour" of being "most graciously" received by Johann Wolfgang von Goethe, then in his 82nd year, who spoke of the newly discovered coral islands of the South Sea. In their published report to the French Minister of Commerce and Public Works and to the Royal Academy of Medicine, Gerardin and Gaimard include the above portraits. The originals are in colour and show on the left a buxom young Austrian woman of 23 with a strawberries-and-cream complexion. In the portrait on the right the complexion has turned to a livid blue-green, allegedly one hour after the subject had been stricken by cholera and three-quarters of an hour before her death. In England the disease was often known as "the blue cholera". Early European observers of cholera were also particularly struck by the mummified appearance of victims of the disease, due to the draining of fluid from the soft tissues. Despite the fact that the cause of death in cholera is massive dehydration, doctors firmly believed that patients should be treated by bleeding. Often the loss of fluid was so great that the blood was of a tarry consistency, and the opening of a vein would produce no result. In such cases, the next step would be to try opening an artery. In 1831 a famous German surgeon, J. F. Dieffenbach, even inserted a catheter into the left ventricle of the heart via the brachial artery in a desperate—but unsuccessful—attempt to obtain blood.² This is the first recorded example of cardiac catheterization. The patient "rendered up his soul" some minutes later. In those days, the cholera patient most likely to survive was the one who could not afford a doctor!

¹ Gerardin, A. & Gaimard, P. (1832), *Du cholera-morbus en Russie, en Prusse et en Autriche pendant les années 1831 et 1832*, Paris.

² Dieffenbach, J. (1832), *Cholera-Archiv*, Bd 1, Ht 1, 86-105.

Asian Steppes. In the following year there was an outbreak at the annual fair of Nižniy Novgorod (now Gorkij), and despite elaborate precautions it soon reached Moscow—the first major European city to be attacked by the disease. In the following years cholera spread to most other European countries, causing calamitous epidemics. At that time quarantine regulations had been devised mainly as a protection against the importation of plague from the Levant. Earlier, yellow fever had made ephemeral appearances on the western seaboard of Europe but had not for some time given cause for alarm. Even plague had been kept at bay for almost a century but was still endemic within the borders of the Ottoman Empire, and the European Powers took elaborate but varying precautions to prevent its importation by maritime traffic with the Levant. As the etiology and mode of spread of plague and cholera were equally shrouded in mystery, similar quarantine precautions were applied to both of them. Such precautions resulted in onerous delays and expenditure occasioned by the immobilization of ships, the incarceration of their crews and passengers in lazarets, and the destruction or spoilage of cargoes.

In the early 1830s the Secretary of the Conseil supérieur de Santé of France, P. de Ségur Dupeyron, was charged by the Minister of Commerce with the responsibility of reporting on the sanitary regulations of the Mediterranean countries. In his report³ in 1834 he pointed to the needless difficulties that arose from differing quarantine requirements by different countries, and proposed that an international meeting should be convened with a view to standardizing protective measures against the importation of exotic diseases. According to Tardieu, writing twenty years later,⁴ the French Government accepted Dupeyron's proposal and attempted unsuccessfully to convene an international conference. But a further French initiative in 1850 succeeded and in this way the long series of International Sanitary Conferences began that were ultimately to lead, almost a century later, to the founding of WHO.

It is of interest to cite some of the procedures that were in force, as described by Papon in 1800.⁵ On disembarking, the Master of an infected or suspected ship was required to stand before an iron grille, swear on oath to tell the truth, and then throw the ship's bill of health into a basin of vinegar. An official would then plunge the bill beneath the surface with the aid of iron tongs and, when it was judged to have been well soaked, remove it by the same means, lay it on the end of a plank, and thus present it to the "conservateur

de la santé", who would read it without touching it. Letters from the unfortunate sick or suspect passengers confined to a lazaret had to be thrown for a distance of ten paces, retrieved with long tongs, plunged into vinegar, and then passed through the flame and smoke of ignited gunpowder. The personnel of the lazaret wore wooden clogs and oilskin jackets, trousers, and gloves.

Very similar precautions were prescribed in regulations promulgated in 1835 by the French Minister of Commerce.⁶ Article 614 stated that where there was need for surgical intervention, a surgical student should be "invited" to be incarcerated with the patient—students presumably being more expendable than doctors. The latter had to be separated from patients with "contagious" diseases by "at least twelve metres" (Article 617), and if the patient was too ill to approach the limit of this no-man's land the doctor would prescribe supposedly suitable remedies on the basis of the report made by the student (Article 618). But another article (616) provided that a surgeon clad in oilskin garments could operate with special long-handled instruments provided that he carried with him a brazier for burning aromatic herbs.

It was firmly believed that low spirits predisposed to epidemic diseases, and Papon cites with apparent approbation the case of a doctor who was "very careful" to drink a few glasses of wine from time to time when attending a potentially dangerous patient. "He did not get drunk," says Papon, "but he became merry."⁷ For the involuntary inmate of a lazaret, the visit of a half-tipsy doctor clad from head to foot in oilskins and bearing long-handled instruments and a portable brazier can hardly have been reassuring!

While these elaborate precautions imposed intolerable constraints upon travellers, what governments found most irksome were the often disastrous hindrances to international commerce, and it was this concern that finally prompted the European nations to meet to discuss to what extent these onerous restrictions could be lifted without undue risk to the health of their populations. If, in the old colonial days, it was true that "trade follows the flag", it was equally true that the first faltering steps towards international health cooperation followed trade.

³ Dupeyron, P. de S. (1834) *Rapport adressé à Son Exc. le Ministre du Commerce*, Paris.

⁴ Tardieu, A. (1854) *Dictionnaire d'hygiène publique et de salubrité*, vol. 3, Paris.

⁵ Papon, J. P. (1800) *De la peste ou les époques de ce fléau et les moyens de s'en préserver*, vol. 2, Paris.

⁶ Toy, J. (1905) *La réglementation de la défense sanitaire contre la peste, le choléra et la fièvre jaune d'après la Convention de Paris 1903*, Paris.

⁷ "Il ne s'enivroit pas; mais il se mettoit en gaité."

The first conference: Paris, 1851

Eleven European States and Turkey were represented at the first of the International Sanitary Conferences. Four of them—the Papal States, Sardinia, Tuscany, and the Two Sicilies—were to become only a few years later part of a unified Italy. The remaining States were Austria, Great Britain, Greece, Portugal, Russia, Spain, and, of course, France, in the dual role of convenor and host.

Each participating country was represented by two delegates—a physician and a diplomat—and it was agreed after some discussion that each government would be entitled to two votes. However, the conference also decided that voting should not be by country but by individual delegates. This curious system was maintained also at the third International Sanitary Conference and often resulted in the anomaly that two delegates of the same country would vote in opposite senses, thus effectively disfranchizing the governments they represented.

In convening this conference, the French Government was inspired by the eminently reasonable desire that international agreement should be reached on the standardization of quarantine regulations aimed at preventing the importation of cholera, plague, and yellow fever (smallpox was then such a universal disease that it was not to be brought within the scope of international sanitary legislation until 76 years later). The situation at the opening of the conference on 23 July⁸ was that plague had long been only a theoretical danger in Europe, and this was even more true of yellow fever, whose European appearances had been, though more recent, ephemeral. Cholera, on the other hand, had within the previous twenty years twice caused havoc and panic not only in Europe but also in the Americas.

Admirable as was the objective underlying this French initiative, its outcome was compromised by inherent and insuperable difficulties; the delegates, whether physicians or diplomats, were equally innocent of any knowledge of the etiology or mode of transmission of the diseases under discussion. Such lack of knowledge was no bar to the holding of convictions that were, within each country, as strong as they were contradictory. There was a

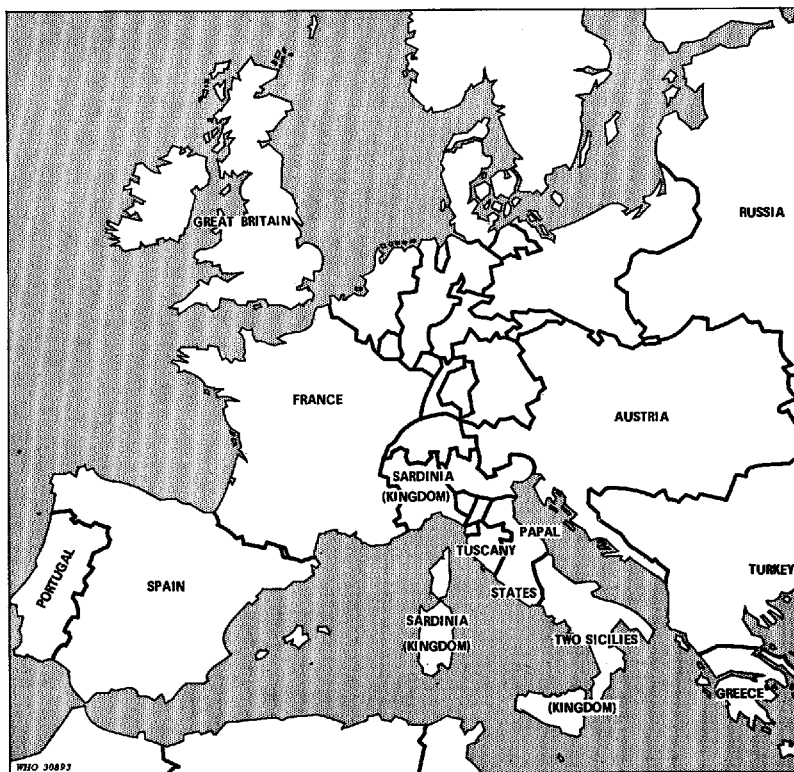
majority view, far from approaching unanimity, that plague and yellow fever were in some way communicable from the sick to the healthy, but it was otherwise with cholera—the only one of the three diseases that had been a recent and terrifying scourge. Early in the debate, the Austrian medical delegate, G. M. Ménis, declared that he was under instructions from his government to discuss only plague and yellow fever. Austria, he said, had tried quarantine measures against cholera which, “far from opposing the ravages of the disease, only made it more frightening and fatal”, and it was the opinion of the most eminent physicians of the Austrian Empire that cholera was “a purely epidemic disease”. In these contentions Ménis received strong support from J. Sutherland, the British medical delegate, who stated that in England cholera was also believed to be “purely epidemic” and that quarantine measures therefore had “no efficacy” against it. That, only two years before, John Snow of London and William Budd of Bristol had, almost simultaneously, postulated that cholera was transmitted by faecally contaminated water was not considered worthy of mention by Sutherland.

To the modern reader the term “a purely epidemic disease” must, in such a context, ring a strange note. But to Ménis, Sutherland, and many of their contemporaries epidemic diseases were not directly or indirectly communicated from the sick to the healthy but simultaneously affected large numbers of persons under the influence of certain atmospheric, climatic, and soil conditions, to which “filth” was often added, the whole forming an “epidemic constitution”. The idea of the transmutability of epidemic diseases was widespread, and some held that plague, yellow fever, cholera, malaria, and typhus were all the same disease, manifesting itself in different guises according to the reigning epidemic constitution.

The question of whether or not cholera was a disease against which quarantine measures could

⁸ In the second edition of *International Health Organizations* (1971) by N. M. Goodman the date is given as 27 July (a Sunday). This is indeed the date that appears on the cover of the printed proceedings. However, the minutes of the inaugural session are clearly dated 23 July, which was also referred to during the closing session as the opening date.

In 1851, when the first International Sanitary Conference opened, the face of Europe wore a very different aspect from that of today. The twelve participating governments were those of Austria, France, Great Britain, Greece, Portugal, Russia, Spain, Turkey (then officially known as "the Sublime Port") and of four Sovereign States that were shortly afterwards to combine to form a united Italy—the Kingdoms of Sardinia and of the Two Sicilies, the Papal States, and Tuscany. The borders of Sardinia then extended as far north as to include part of what is now a suburb of Geneva. This was essentially the Europe as mapped out by the Congress of Vienna in 1815. Opening the 1851 Conference, the French Foreign Minister referred to the International Exhibition in London in the same year as heralding a new age of industrial cooperation between nations. In the same year also, telegraphic communications were established between London and Paris.



have any effect was too thorny for immediate discussion in plenary session and the conference therefore appointed a committee of seven members—four physicians and three diplomats—to study and report on it. Introducing the committee's report, its secretary, Mèlier, of France, stressed at the ninth plenary session of the conference that it had excluded not only all political questions but also any discussion of scientific theory. (One can only wonder what was left!) Indeed, he said, the words *contagion* and *infection*, "which had occasioned so many arguments elsewhere", had not even been mentioned. If, in preparing the agenda for the conference, Mèlier explained, France had included cholera with plague and yellow fever as one of the diseases to be subject to quarantine, it was not because of a belief that this served a useful purpose but "as a satisfaction given by France to an opinion that still prevails elsewhere". Mèlier then summarized the conclusions of the committee. By a majority of four to three it had decided that, in the case of cholera, it was "humanly impossible to do anything useful or efficacious against such a scourge", which "fell like a storm on the country that it reached". Quarantine measures against cholera were "impossible, illusory, even dangerous

in certain cases, and contrary to the end for which they were intended".

The conference was to last for no less than six months. Exactly two months after its opening it met in plenary session to discuss the committee's report and decide whether cholera was susceptible to quarantine measures and therefore eligible for inclusion in the proposed international sanitary regulations. This discussion, lasting three and a half hours, took place on 23 September 1851, and it was agreed to adjourn it until four days later, when Mèlier summarized the rival points of view as follows. Three of the four Italian Powers—the Papal States, Tuscany, and the Two Sicilies—advocated quarantine measures against cholera. For them, epidemicity was nothing, and importation everything. The fourth—Sardinia—was in the opposite camp, as were Austria, Britain, and France, which were unanimous in declaring the impotence of *cordons sanitaires* and of maritime quarantine against cholera.

At this point, the Spanish medical delegate, Pedro F. Monlau, intervened. Admitting that cholera was not "constantly, essentially, and universally contagious", that quarantine caused loss of time, and that, as the English said, "time

Berliner Cholera-Zeitung

mit

Benutzung amtlicher Quellen;

herausgegeben

von

einem Verein von Medicinal-Beamten.

Desinficirt.

N^o 1.

Sonnabend den 24. September.

1831.

Ankündigung und Plan dieser Zeitung.

Das Bedürfnis, das hiesige Publikum über den täglichen Stand und Gang der Cholera in unserer Stadt durch specielle Nachweisung der Ergebnisse der Erkrankungen, Genesungen und Sterbefälle, wie der fortwährend zur Hemmung der Seuche erwiderten Maßregeln in genauester wenn auch nur durch treue Darstellung der Thatfachen und Veröffentlichung täglich erneuter Gerüchte, durch Erläuterung und Beleuchtung so mancher Verhältnisse, die hier und da wohl dem Nicht-Sachkenner heurührender erscheinen, als es möglich sind, etwas bekannt zu machen.

The dramatic impact of cholera is strikingly illustrated by the sudden vast output of publications on it during the successive occasions when it overran Europe. As early as 1831, Jaehnichen of Moscow wrote: "Since Divine Providence has delivered the town from the scourge of cholera, its inhabitants find themselves afflicted by another calamity: the works that authors rush to publish, one by one, on the fatal disease." The third volume of the first series of the *Index-Catalogue of the Library of the Surgeon-General's Office* (1882) lists 15 journals solely devoted to cholera, of which 12 were started in 1831 or 1832. The illustration shows one of these. On the first page of each issue the word DESINFICIRT ("disinfected") was printed. The same volume of the *Index-Catalogue* lists separately publications on cholera before and after 1817—the year when the first cholera pandemic started. For the years 1666-1816 there are 66 publications, most of which have nothing to do with the disease that we now know as cholera. For the years 1817-1881 there are 150 pages of entries representing over 7000 publications.

Photo by courtesy of the National Library of Medicine, Bethesda, Md., USA

is money", he pointed out that "public health is gold", and in a long peroration pleaded that cholera should not be excluded from quarantine regulations. Then followed Anthony Perrier, the British diplomatic delegate, who enumerated the names of no less than twenty-six distinguished French physicians who had declared themselves against the communicability of cholera, and cited examples of anti-contagionist opinions in Austria, Russia, and Spain. In England, he asserted, a report was in preparation in which it would be said that "contagion is not a fact, but an hypothesis invented to explain a number of facts that, without this hypothesis, would be inexplicable". To the modern reader, an hypothesis that explains otherwise inexplicable facts would have some claim to attention. Not so for Perrier, who said:

It seems to me that there is an obstinate determination on the part of some of our honourable colleagues to persist in the routine path of practices that are outmoded, useless, ruinous to commerce, and harmful to public health, in that, instead of enlightening the peoples on the true means of guaranteeing themselves against epidemics, they inspire, on the contrary, a false sense of security that prevents them from taking the only sanitary precautions that can offer real guarantees. In short, I seem to see some serious and respectable men who, instead of spreading the light unveiled by the progress of science, would like to revive and perpetuate practices followed under the influence of past centuries. God will that I am mistaken, that the fear of a deplorable cleavage has exaggerated the evil in my eyes, and that the truth may finish by triumphing.

Perrier concluded his eloquent appeal with the hope that the conference would not finish by "an

abortion that would cover it with ridicule in the eyes of the civilized world".

Spanish, Greek, and Tuscan delegates then pronounced themselves in favour of quarantine against cholera, while the medical delegate of Portugal proposed one of those harmless non-resolutions that are not entirely foreign to modern international affairs. Lamenting the lack of understanding of the disease "that God seems to have sent us to confound the pride of human knowledge", he suggested that quarantine for cholera should be "optional" and "of a duration less than that for yellow fever". Further, "suitable measures" should be taken to destroy the epidemic constitution of the disease "to the extent that is possible". The adoption of such a resolution would have given cause to wonder why the conference had ever been held!

It was now the turn of the Russian medical delegate, Carlos O. R. Rosenberger, who referred to the first invasion of his country by cholera in 1829-32. Very severe quarantine regulations were then in force but nevertheless almost 290 000 Russians had perished from the disease. This appalling mortality had discredited quarantine measures. However, during the second invasion by cholera—from late 1846 to 1849—when quarantine was not enforced, more than 880 000 Russians had succumbed to the disease. These statistics, and apparently clear instances of communication of the disease from the sick to the healthy, had caused the Russian Government to think again in terms of quarantine precautions.

This was too much for Ménis, of Austria, who outdid even Perrier in his anti-contagionist eloquence. The great difference between plague and cholera, he said, was that the former attacked all sorts and conditions of people. Cholera, on the other hand, selected principally the dregs of society, including the intemperate, the debauched, decrepit old men, those languishing from long illnesses, the insane, and the imprudent and timorous. The best weapons against it were courage, resignation, spiritual calmness, and faith. Cholera could be thought of as a divine wind sent on earth to punish those who did not know how to look after their own health. Properly considered by governments and doctors, it could serve to make men better by reforming their morals and habits. It was a scourge sent not to wipe out humanity but to punish and correct it. He concluded by declaiming that quarantine against cholera was not only useless but eminently dangerous to the conservation and the civilization of peoples. Ménis was not alone in attributing a beneficent influence to cholera. Twenty years before, Sir Gilbert Blane in England

had spoken of its "horrible torments" as being "of equal potency with the gallows as a dissuasive to vice, certainly far more terrible than transportation for life". For Blane, it was the duty of doctors to advise the clergy of "the power of the instrument which is put into their hands".⁹

The conference discussions continued but were interrupted by the arrival, over ten weeks late, of the Turkish medical delegate, who coolly requested that the debate be adjourned to enable him to study the documents. This request was accorded, and the conference resumed its work two days later. After a brief discussion the Chairman put to the vote the question whether or not cholera should be subject to quarantine regulations. Of twenty-three delegates present, fifteen voted in the affirmative, four were against, and four abstained. Thus, after fierce opposition, did cholera gain admission to the quarantine club.

The practical result of this majority decision, as of all the decisions of the conference, was nil. Agreement was reached on the text of a draft Sanitary Convention (*Projet de Convention sanitaire*) and annexed draft International Sanitary Regulations (*Projet de Règlement sanitaire international*) consisting of 137 articles, but these were pieces of prose that committed none of the participating governments unless they subsequently ratified them.

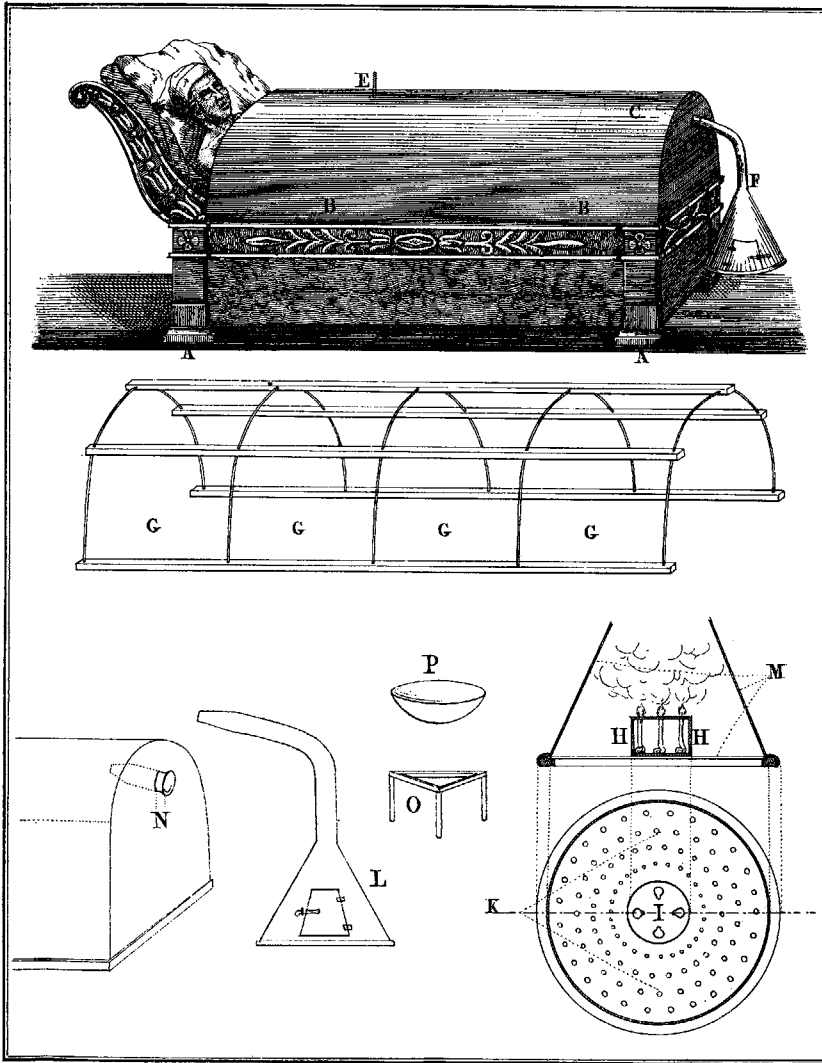
At the closing session of the conference the French Minister of Foreign Affairs congratulated the delegates on having "gloriously accomplished" their mission. The fact that they had taken six months to achieve what was in reality nothing showed that they had understood that time was precious, and they had completed in this short time—"illuminated by the torch of science"—a task that might well have taken years.

On 27 May 1853 the Emperor Napoleon III of France issued an Imperial Decree promulgating the "International Sanitary Convention concluded between France, Sardinia, and various other maritime Powers".¹⁰ It is clear from the text of this decree that Sardinia was the only country to have exchanged—on 18 May 1853—acts of ratification with France (which were denounced a few years later). Adrien Proust, one of the leading participants in the International Sanitary Conferences, stated in 1873 that Portugal also ratified the convention, citing as his authority the Imperial Decree of 27 May 1853.¹¹ Several later writers have repeated

⁹ Blane, G. (1831) *Warning to the British public against the alarming approach of the Indian cholera*, London.

¹⁰ France. Ministère de l'Agriculture, du Commerce et des travaux publics. *Acte et instructions pour l'exécution de la Convention sanitaire internationale* [Paris, 1853].

¹¹ Proust, A. (1873) *Essai sur l'hygiène internationale*, Paris.



In 1831 Professor H. Scoutetten of Strasbourg was sent by his health department to Berlin to investigate the cholera epidemic raging in that city. In his published account of his findings he includes this plate, which represents a special bed for treating cholera patients by heat.¹² The funnel-shaped device protruding from the foot of the bed contains a spirit lamp with four wicks, as shown in the cross-section lettered M. The base of the device contains many perforations, as shown in K. P and O are respectively a bowl and tripod that could be placed over the lamp for vaporizing aromatic herbs or sulfur. While some doctors believed in treating cholera by the application of heat, others were equally convinced that cold should be applied. The latter gave their patients ice to suck and cold enemas, and sometimes even hosed them with cold water. Whether a patient was roasted or refrigerated depended on his choice of medical attendant.

WHO photograph from original in the author's possession

Proust's statement, but in fact although Portugal signed the decree it did not ratify its signature.

Thus, from the point of view of practical results, the first International Sanitary Conference was a fiasco. Everyone went on doing in their own way what they had done before. Yet there was more to it than that. The fact that the conference took place established the principle that health protection was a proper subject for international consultations even though international health cooper-

ation was for many years to be limited to defensive quarantine measures. The French Government of the time had planted a seed that was not to germinate for some forty years and then, after a complicated cycle of development, to blossom more than half a century later into the World Health Organization.

¹² Scoutetten, H. *Relation historique et médicale de l'épidémie de choléra qui a régné à Berlin en 1831*. Paris, 1832.

The second conference: Paris, 1859

In the eight-year interval between the first and second of the International Sanitary Conferences there appeared two publications that, taken together, provided the complete answer to the enigma of cholera. It was to be many years before the crucial importance of one of them was to be generally recognized, while the other has been almost universally overlooked. The authors of these pioneer observations were Filippo Pacini (1812-1883) of Florence, a microscopist, and John Snow (1813-1858) of London, an anaesthetist and, in his spare time, an epidemiologist.

While in all the standard works on bacteriology and medical history Robert Koch is credited with the incrimination of the cholera vibrio as the pathogen of the disease, Pacini anticipated him by thirty years when he published in 1854 (in Italian) his "Microscopic observations and pathologic deductions on Asiatic cholera".¹³ In this monograph Pacini described numerous vibrios seen in the intestinal contents of three cholera victims and, in a fourth victim, he was struck by their "enormous quantity", especially in the flocculi consisting of mucus and desquamated epithelial cells. "When I pulled these masses of cells apart a little under the microscope, myriads of vibrios emerged...". Referring to the characteristic appearances of the small intestine in cholera victims, Pacini added: "...in spite of the most precise and meticulous search, we have not come across anything that could be considered capable of producing the epithelial desquamation [now considered a post-mortem change] and other changes but the millions of vibrios that are found in the intestines".

Pacini recognized that there were morphologically similar vibrios that could live in various parts of the human body without apparent harm, but he considered that what he called the "vibrio cholera" was an unusual species that was constantly associated with the disease. He emphasized, in capital letters, that a contagion was an "ORGANIC, LIVING, SUBSTANCE OF A PARASITIC NATURE, WHICH CAN COMMUNICATE ITSELF, REPRODUCE ITSELF, AND THEREBY PRODUCE A SPECIFIC DISEASE". For many years Pacini fought a lone and unsuccessful battle for the recognition of the vibrio as the cholera

pathogen, once remarking bitterly that his countrymen would accept his discovery only when a foreigner had repeated it. He was not so pessimistic as to foresee that the foreigner who did repeat the discovery would get the sole credit for it.

Pacini was not alone in identifying the cholera vibrio in 1854, for in that year a London microscopist, Arthur Hill Hassall, reported to the Medical Council of the General Board of Health, strangely enough using the same expression as Pacini's, that he had seen "myriads of vibriones" in "every drop of every sample of rice-water discharges".¹⁴ However, neither he nor the General Board of Health appreciated, as did Pacini, the etiological significance of the vibrios.

Also in London, the epidemiological investigations of John Snow provided the perfect complement to Pacini's pioneer microscopical researches. His 1849 publication had been a mere pamphlet of 31 pages,¹⁵ but the so-called second edition that he published in 1855 was in fact a new book in which he reported much more elaborate and refined epidemiological investigations correlating cholera incidence and water supplies in London in 1854.¹⁶ Snow's work has long been recognized as a classic, and it would be superfluous to summarize it here. But it is difficult to understand how his impeccable reasoning could have made so little impact on his contemporaries. William Farr considered Snow's observations to be of importance, but regarded them as pointing to one possible mode of transmission of cholera. In a report to the General Board of Health, the great John Simon referred in 1858 to Snow's "peculiar doctrine (first advanced in 1849) as to the contagiousness of cholera... Against this doctrine almost insuperable arguments have been stated... Dr Snow's illustrations are very far from proving his doctrine: but they are valuable evidence of the danger of drinking fecal-

¹³ Pacini, F. (1854) *Gazz. med. ital. tosc.*, 2nd ser., 6, 397, 405.

¹⁴ Hassall, A. H. (1855) In: Great Britain, General Board of Health, *Report of the Committee for Scientific Enquiries in relation to the Cholera Epidemic of 1854*, London.

¹⁵ Snow, J. (1849) *On the mode of communication of cholera*, London.

¹⁶ Snow, J. (1855) *On the mode of communication of cholera*, 2nd ed., London.

SOUVENIRS DU CHOLÉRA-MORBUS.



A census made in 1831 showed that the inhabitants of Paris numbered 785 862. On 26 March 1832 cholera struck the city for the first time in its history, the infection having come from England. In April 1832 alone there were 12 733 deaths from cholera in Paris. This was more than half the average annual number of deaths from all causes for the previous ten years, and an intolerable strain was placed upon public services. There was a penury not only of gravediggers but also of transport to take the dead to the burial grounds. An attempt was made to remedy the latter deficiency by pressing military wagons into service, but this solution had to be abandoned for two reasons: the vehicles were unsprung, and the noise that they made at night in the cobbled streets of the city deprived the inhabitants of sleep and added to the reigning atmosphere of terror. Moreover, the vibration was such that the coffins disintegrated and foul fluids escaped from the corpses. This experiment was abandoned after only one day. The epidemic ended in September, having claimed a total of 18 402 victims.¹⁷ Thanks to cholera, deaths in Paris in 1832 jumped from an expected 23 000 to 44 119. In this drawing by a famous artist, Daumier, the man in the foreground has collapsed in the street from cholera. In the background, two men are carrying a coffin while a hearse drives by bearing another. On the left, a terrified woman rushes into the house, while on the right even the dog has its tail between its legs.

¹⁷ *Rapport sur la marche et les effets du choléra-morbis dans Paris et les communes rurales du département de la Seine*, Paris, Imprimerie Royale, 1834.



One year after the first International Sanitary Conference, *Punch* published this cartoon entitled "A Court for King Cholera". Britain had then suffered from two disastrous waves of the disease, and was to have two more. While the nature of cholera, as of other diseases, remained an enigma, there was a general recognition that insanitary conditions predisposed to disease. The title of the cartoon is a pun, for the "courts" were small rectangular open spaces bounded by slum dwellings in which the inhabitants lived in conditions of unimaginable squalor and overcrowding. Such conditions provided the ideal soil for the spread of cholera, as of other communicable diseases. Unhappily, comparable conditions still exist in some countries, and it is only in these that cholera continues to constitute a menace. The elucidation of the etiology of cholera did little or nothing to aid in its prevention for it had been recognized long before—if for the wrong reasons—that the surest shield against the disease was a pure supply of piped water and the sanitary disposal of human wastes.

WHO photograph from original
in the author's possession

ized water during the epidemic prevalence of cholera".¹⁸

In Germany, Max von Pettenkofer of Munich derided the "drinking-water theory" as from 1855,¹⁹ and he and then his followers continued to do so for over half a century. In France, Snow fared no better. A wealthy industrial chemist, Jean-Robert Bréant, had at the height of the 1849 cholera epidemic in Paris executed a will in which he

bequeathed to the Paris Academy of Sciences the sum of 100 000 francs to be awarded to whomsoever should find a cure for cholera or discover its cause. Bréant also provided that until such time as the prize was awarded the interest on the

¹⁸ Simon, J. (1858) In: Great Britain, General Board of Health, *Papers relating to the sanitary state of the people of England*, London.

¹⁹ Pettenkofer, M. von (1855) *Untersuchungen und Beobachtungen über die Verbreitungsart der Cholera*, München.

capital sum should be used for an annual prize to "the person who will have advanced science on the question of cholera or any other epidemic disease. . .".²⁰ In 1852 Bréant died, and in the following year the Minister of Education transmitted to the Academy an Imperial Decree authorizing acceptance of the bequest (the *Legs Bréant*). The Academy thereupon appointed a committee, which included Claude Bernard and Alfred Armand L.-P. Velpeau, to judge the entries. By May 1858, 153 communications, coming not only from France but from eight other countries, had been received.²¹ Pacini submitted his published study of 1854 on the cholera vibrio²² and Snow his of the following year on the epidemiology of the disease.²³ These two contributions, which should have been epoch-making, were not—as was the case with Gregor Mendel's fundamental studies in plant genetics some ten years later—published in an obscure provincial journal, thus escaping notice until many years later. They were discussed in their countries of origin, brought to the attention of the Paris Academy of Sciences, and repudiated. Instead, the Academy retained for special mention two contributions "whose authors have properly understood the real aim of this competition, by limiting themselves to indicating specific measures for the cure of cholera". One of the authors was a Russian, the Chief Physician to the hospital of Smolensk, who maintained that the "virus" of cholera was identical with that of typhus, typhoid fever, and smallpox. It followed, he argued, that cholera patients should be treated by the inoculation of smallpox pus. The other, an English physician in private practice, claimed outstanding results by the oral administration of very small doses of calomel very frequently—usually one grain every five minutes.²⁴ In neither case did the Academy consider that these contributions merited the award which, in fact, was never made. However, many annual Bréant prizes were awarded, and continue to be until this day.

John Snow's contribution has long been recognized as a milestone in medical history, but it was not until 1965 that belated recognition was accorded to Pacini by his peers when the Judicial Committee of the International Committee on Bacteriological Nomenclature ruled that the cholera vibrio should be known as "*Vibrio cholerae* Pacini 1854".²⁵

Such was the background to the second International Conference, which opened in Paris on April 9 1859 and for which France again played the dual role of convenor and host. This conference was essentially a replay of its predecessor, and France was evidently inspired by the idea that

something might be salvaged from all the work that had gone into the previous conference if the countries concerned could discuss matters at a purely diplomatic level and, perhaps, be aided in such discussions by having before them a revised and simplified text of the agreement that had previously been rejected. To this end, participating countries had been invited to send only a diplomatic delegate and, as a basis for discussion, France had prepared a simpler "draft convention" that was essentially an amalgamation into one document of the convention and the annexed international sanitary regulations elaborated by the first conference. The countries represented at the conference were the same as before, with the exception of the Kingdom of the Two Sicilies, which at that time did not enjoy diplomatic relations with France. The Austrian delegate withdrew on 30 April on the outbreak of war between Austria and France, but returned on 20 August and remained until the closing session on the 30th of the same month. The Tuscan delegate attended for roughly the first third of the proceedings and then disappeared permanently from the scene.

When the conference closed it had lasted for five months. Its outcome was that Austria, France, Great Britain, the Papal States, Portugal, Russia, Sardinia, and Spain signed the slightly amended "draft convention", while Greece and Turkey abstained. This convention was never ratified by any of the participating States. As might be expected from the composition of the conference, its scientific content was negligible, the only point of medical interest being that the differences between contagionists and anti-contagionists in regard to cholera were as wide as ever, if not more so. The two men—Pacini and Snow—who only four or five years before had jointly provided a complete solution to their sterile polemics, were not even mentioned.

The British delegate, reflecting the views of official medicine in his country, had moved that cholera should be omitted from the diseases to be subject to regulations. Experience acquired since the 1851 conference, he said, had

more and more shown that this disease is not contagious at all, and that, from another point of view, the development of European railway networks in the meantime today renders illusory any system of quarantine against arrivals by sea from cholera-infected places.

²⁰ *C.R. Acad. Sci. Paris*, 1854, 39, 995.

²¹ *C.R. Acad. Sci. Paris*, 1858, 46, 1031.

²² *C.R. Acad. Sci. Paris*, 1855, 40, 30.

²³ *C.R. Acad. Sci. Paris*, 1855, 41, 647.

²⁴ Ayre, J. (1859) *A memoir on the treatment of epidemic cholera read before the Members of the French Academy of Sciences*, London.

²⁵ *Internat. Bull. bact. Nomencl.*, 1965, 15, 185.



FARADAY GIVING HIS CARD TO FATHER THAMES;

And we hope the Dirty Fellow will consult the learned Professor.

In 1855 Michael Faraday, the great English scientist whose name is immortalized in that of the international unit of electrical capacity—the farad—sent a letter to *The Times* protesting against the appalling pollution of the river Thames. Its water, said Faraday, was of an “opaque pale brown” colour, and a piece of white card that he had thrown into it became invisible at a very small degree of submersion. *Punch*, the English satirical weekly founded in 1841 and originally modelled on the French *Charivari*, represented Faraday’s simple experiment in graphic form in this cartoon published on 21 July 1855, at the same time expressing the hope that “Faraday’s epistle” would help to avert cholera. It was in the same year that John Snow published the second edition of *On the Mode of Communication of Cholera*, the importance of which was generally overlooked in his own and in other countries, although it is now recognized as a classic of valid epidemiological reasoning. While England was the birthplace of environmental sanitation, the English sanitarians obstinately refused to believe for many years the simple truths that Snow’s investigations had revealed. Nevertheless, they were firmly convinced that the provision of pure water supplies and the sanitary disposal of human wastes contributed in some indefinable way to health. Immense sums of money were spent on sanitary improvements, with the result that the British Isles became free from cholera epidemics some three decades before other Western European countries.

WHO photograph from original
in the author’s possession

The Austrian and Sardinian delegates then declared that they also would have liked to suppress the references to cholera but that, in order to facilitate general agreement, they proposed to vote an "optional" quarantine against the disease. Greece, the Papal States, Portugal, and Spain reluctantly agreed to this face-saving formula, while affirming their preference that quarantine against cholera should be obligatory. At last, a rather hollow agreement seemed to have been reached, but ten sessions later, Great Britain—supported by Russia and Sardinia—declared its belief that, by reason of the mode of propagation of the disease, any quarantine against cholera was "entirely illusory". On two further occasions Great Britain intervened to protest the futility of quarantine against cholera, and in the last few days of the conference the Austrian delegate, who had resumed participation the day before and therefore missed all the arguments and counter-arguments, moved that cholera should be excluded from the diseases

whose presence aboard could lead to the detention of a ship.

A stage had been reached when the only thing to do was to put the motion to the vote. Delegates of ten countries were present and, of these, five voted for the motion and five against. This deadlock was solved by agreeing to regard the chairman as having the casting vote. He had voted against, and the motion was therefore lost. Had the voting been in the opposite sense it would have made no difference. The participants dispersed and returned to their own countries, doubtless bearing their copies of the draft convention, which were duly filed and duly forgotten.

In the space of nine years, the first two International Sanitary Conferences had involved a total of eleven months of fruitless discussions. Nevertheless, an important precedent had been set. In future years, an ever-increasing number of nations were to realize that an ever-increasing number of health problems called for agreement at the international level.

The third conference: Constantinople, 1866

Once again, it was the French Government that took the initiative in calling for a third International Sanitary Conference, the main motivation being provided by the invasion of Europe in 1865 by cholera, which, for the first time in recorded history, had been imported across the Mediterranean from Egypt. The French Foreign Minister and the Minister of Agriculture, Commerce, and Public Works had on 5 October 1865 jointly addressed a memorandum to the Emperor, in which they proposed that France should suggest to the other interested Powers that a "diplomatic conference" be convened in the near future to consider the conclusions to be drawn from the latest invasion of Europe by cholera and the means to be taken to prevent a repetition of such incursions. The Emperor agreed, and on 13 October the Foreign Minister addressed a circular letter to diplomatic missions in Paris inviting their countries' participation in a conference at which delegates of the Powers should be accompanied by "men of science judged the best qualified to clarify its deliberations by their special insights". This time it was proposed that the conference should be held not in Paris but in Constantinople. The Turkish Government acceded to this proposal and sent invitations to 16 other governments, of which all but one—the United States of America—accepted.

The conference opened in Constantinople on 13 February 1866. Sardinia, Tuscany, and the Two Sicilies had by then been incorporated into a united Italy, but the Papal States were still separately represented. All the other Powers that had participated in the first two conferences were present and, in addition, Belgium, Denmark, the Netherlands, Persia, Prussia, and Sweden/Norway (then politically united) made their first appearance. The conference set several notable precedents: it was devoted exclusively to cholera; it was the longest of the International Sanitary Conferences, lasting for seven months; and it was the first of the conferences to reach a considerable measure of apparent agreement on some basic questions. Moreover, as

pointed out by the medical delegate of Portugal at the seventh session, it differed in an important respect from its two predecessors, in that

today we see things from a more general and more philosophic point of view, and we wish to combat the scourge in the very countries in which it is born or, at least, to halt its progress as near as possible to its original home.

Once again it was decided that voting should be by individuals instead of by countries, and that each country should be entitled to not more than two votes. Delegates in excess of two were allowed to participate in the discussions without voting rights. This system theoretically put one-man delegations at a disadvantage, but as delegates of the same countries often voted in opposite senses, one vote could, paradoxically, prove to be more effective than two.

The climate of opinion at the time of the conference

On the eve of the conference there were still profound differences of opinion as to the nature and mode of spread of major epidemic diseases. In Bavaria, Pettenkofer was slowly building up his elaborate theories of the epidemiology of cholera and other epidemic diseases, which put him at mid-point between contagionists and anti-contagionists. It was undeniable, he said, that cholera was spread by the movements of people, and it was now making its third "great expedition" from India. But human travel was not the only factor. For the disease to become epidemic, a certain condition of the soil was necessary, and cholera—like malaria and typhoid—was a soil-disease (*Bodenkrankheit*).²⁶ Referring to Snow's contention that cholera was spread by drinking-water—which he still hotly disputed—Pettenkofer pointed out that the same water was also used for domestic purposes, and that substantial amounts of it therefore came into contact with the soil. Summarizing in 1865 the elements necessary for the development of a cholera epidemic, he asserted that they comprised:

²⁶ *Z. Biol.*, 1865, 1, 322.

PROCÈS-VERBAUX

DE LA

CONFÉRENCE SANITAIRE INTERNATIONALE

OUVERTE A CONSTANTINOPLÉ

LE 13 FÉVRIER 1866

TOME I.

CONSTANTINOPLÉ
—
IMPRIMERIE CENTRALE
—
1866.

The third International Sanitary Conference in Constantinople in 1866 was remarkable in several respects. Apart from the anomalous 1881 conference in Washington it was the only one not to be held in Western Europe. It was by far the longest in duration of these conferences, opening on 13 February and closing on 26 September. Its printed proceedings, which run to 1130 pages, are very rare, and according to a standard reference work on international conference proceedings the only copy located in the whole of North America is in the University of Michigan. Cholera had hitherto spread slowly by land from India across the Asian steppes to southern Russia and then to the rest of Europe, but in 1865 it was conveyed by sea from Egypt to Mediterranean ports in Europe, whence it spread. It was this new outbreak that prompted the convening of the Constantinople conference. As with the two preceding and the three succeeding conferences, no international treaty resulted. After discussions lasting for over seven months, delegates returned to their countries by the slow means then available, agreeing on certain points but disagreeing on others. Cholera had been the sole subject of discussion at this conference, but while all delegates were ignorant of its causes any hope of international agreement remained illusory. The contrast between this conference only just over a century ago and the annual meetings of the World Health Assembly could hardly be more striking. The Assembly lasts for just under three weeks, and delegates from almost 140 countries come by jetplane, decide on a worldwide programme and its budget, and are soon back again at their normal occupations.

(1) an inhabited stratum of soil that was porous to water and air to the level of the ground-water;

(2) temporary fluctuations in the moisture of this stratum, the most dangerous period being when the ground-water had sunk from an abnormally high level;

(3) the presence in the soil of excrementitious matter;

(4) the specific germ (*Keim*) of cholera, which was principally conveyed by the excrement of

cholera patients, and possibly also by that of healthy subjects who had come from a cholera-infected area;

(5) an individual susceptibility to cholera.

The germ, he said, must be of an organic nature, and be either a cell or a ferment, and the question arose whether it was present only in the excrement of cholera patients or also in that of subjects who were free of symptoms. He concluded: "We have no grounds for exonerating the latter."

In the same year the Harveian Medical Society of London organized a debate on cholera, because "so great a difference of opinion" existed as to its contagiousness.²⁷ Of 13 speakers, 7 declared for contagion and 5 against. The remaining speaker's contribution was reported as follows:

Although a non-contagionist, he thought the specific poison was undoubtedly conveyed through individuals arriving from infected places, and that attendants on cholera patients were not infrequently attacked. Hence, strict quarantine regulations should be enforced on vessels from infected places. Those attacked also should be perfectly isolated, and a *cordon sanitaire* should be kept up.

The above quotation, as also the summary of Pectenker's contentions, illustrates how artificial is the absolute distinction commonly drawn between contagionists and non-contagionists, or contagionists and miasmatisers. The terms "germ", "miasm", "animalcule", "microphyte", "seed", "fungus", "virus", and "insect" were used interchangeably, and between the extreme contagionists and the extreme anti-contagionists there was a whole spectrum of shades of opinion. In the course of the discussion at the Harveian Medical Society, one of the latter declared that he "would not be afraid to drink a pint" of rice-water evacuations, whereupon a contagionist colleague pleaded with him not to run the risk of this "noble and heroic" gastronomic exercise.

Among the French, the most influential anti-contagionist of the time was A. B. Clot—generally known as Clot Bey—who was Chief Physician to the Viceroy of Egypt and Inspector-General of the Egyptian civil and military medical services. For over thirty years Clot Bey had insisted on the non-contagiousness of plague, and applied the same reasoning to cholera and yellow fever. In 1835 he had, in the presence of several physicians, pharmacists, and public officials, inoculated himself in the arm with pus from a bubo of a plague patient in a Cairo hospital, without suffering any ill effects. In 1866, the year of the third International Sanitary Conference, he published his fourth book on plague under the title "Last Words on the Non-Contagion of Plague".²⁸ In the preface to this work he speaks approvingly of the influence of anti-contagionist ideas at the first International Sanitary Conference fifteen years earlier, but laments that contagionism has since taken a new hold:

This return to ideas renovated from the Middle Ages seems to me deplorable and unworthy of our epoch. After having combated it in regard to cholera, I believe it to be my duty to combat it in regard to plague, which, according to my experience and deep conviction, is an epidemic and not a contagious disease.

Even had Clot Bey's experiment on himself resulted in his contracting a non-fatal plague infection, his convictions would not necessarily have been shaken. Years before, a prominent English anti-contagionist, C. Maclean, had proceeded to Constantinople and, to demonstrate the truth of his views, taken up residence in the Greek Pest Hospital and immediately assumed responsibility for the medical care of its patients. After only five days Maclean himself became seriously ill with plague, but strenuously repudiated the suggestion that this may have been a consequence of direct or indirect contact with plague patients. Another experimenter on himself was a Dr Douglas Whyte who, in the Pest House of the Indian Army at El Hammid in Egypt, inoculated himself in the wrist with pus from a bubo, fell ill on the fourth day, and died on the seventh. For Maclean, this was a pure coincidence. Asked in 1819 by a parliamentary Select Committee on plague how he thought that he himself had contracted the disease, he replied "by the air". He also maintained that the calamitous epidemic of plague in Britain in 1665 was not "the Levant plague", because an epidemic disease could not be conveyed from one country to another.²⁹

The ferocity of Maclean's rebuttal of the doctrine of contagion knew no bounds. Writing in 1818 he asserted that the "fraudulent origin of this pernicious error" was to be found in the publication in 1546 by Fracastorius of his *De Contagione*. Fracastorius, said Maclean, was "a mere creature of the Pope".³⁰ Five years later he wrote that quarantine was "the most gigantic, extraordinary, and mischievous superstructure, that has ever been raised by man, upon a purely imaginary foundation", and that the doctrine of contagion was a "pious fraud", the purpose of which was to "create a pretext for the translation of the Council of Trent to Bologna".³¹ Fracastorius was, in fact, physician to the Council of Trent, and there was some kind of epidemic there. In the mind of Maclean these circumstances furnished sufficient reason to suppose that Pope Paul III had bribed Fracastorius to invent the idea of contagion in order to persuade the Council to transfer the seat of its deliberations!

²⁷ Drysdale, C., ed. (1866) *On cholera: its nature and treatment, being the debate in the Harveian Medical Society of London*, London.

²⁸ Clot, A. B. (1866) *Derniers mots sur la non-contagion de la peste*, Paris.

²⁹ Great Britain, Parliament, House of Commons (1819) *Report from the Select Committee appointed to consider the validity of the doctrine of contagion in plague*, London.

³⁰ Maclean, C. (1818) *Results of an investigation respecting epidemic and pestilential diseases; including researches in the Levant concerning the plague*, London.

³¹ Maclean, C. (1823) *Remarks on the British quarantine, and the so-called sanitary laws of the continental nations of Europe, especially those of Spain*, London.



National Library of Medicine, Bethesda, Md., USA

In 1825 Antoine-Barthelmy Clot (1793–1868), a French physician, was appointed by the Viceroy of Egypt, Mohammed-Ali, as chief of the medical service of the Egyptian army. This appointment was only one of many examples of Mohammed-Ali's farsighted efforts to modernize Egypt by the introduction of European science and technology. Clot founded the Cairo medical school and completely identified himself with Egyptian life and aspirations. In 1832 he was awarded the title Bey and henceforth became known not only in Egypt but throughout Europe as Clot Bey. He habitually wore contemporary Egyptian dress, even on European visits, and when he visited London in 1833 the *Lancet* published a full-page portrait of him thus attired, together with a highly laudatory account of his work in Egypt. In 1832 Clot Bey had published an account of cholera in Arabia and Egypt. In 1840 he published another on plague in Egypt, and in 1866—the year of the third International Sanitary Conference and two years before his death—he published his “last words on the non-contagion of the plague” (*Derniers mots sur la non-contagion de la Peste*). Clot Bey had a fanatical belief that neither cholera nor plague were communicable diseases. He sought to demonstrate the truth of his convictions by inoculating himself on 15 March 1835 with pus from the bubo of a plague patient in a Cairo hospital. As shown in the above picture, taken from Clot Bey's 1866 publication, this demonstration was witnessed by several doctors, pharmacists, and public officials. Clot Bey suffered no ill effects but an English doctor, Douglas Whyte, who had made a similar auto-experiment in Egypt a few years before, died of the disease seven days later. Another obsessional anti-contagionist, Dr Charles Maclean, testified before a British parliamentary committee on plague in 1819 and affirmed that the unfortunate outcome of Whyte's experiment was a pure coincidence. The tenacity with which such beliefs were held in many countries hardly favoured international agreement on international quarantine measures.

Both contagionists and anti-contagionists made up their minds first and then selected the facts that seemed to fit their theories. A much discussed question was whether the incidence of cholera was higher in hospital personnel than in the population at large. Anti-contagionists could find many examples to show that the incidence among hospital personnel was the same as or even lower than among the general population. Contagionists

could find many examples to the contrary, but even when confronted with these examples anti-contagionists would find support in them for their own theories. Thus, Jaehnichen, physician to the first administrative district of Moscow during the cholera epidemics of 1830 and 1831 in that city, interpreted a mortality of 30% in hospital personnel as compared with only 3% in the general population as providing an argument *against* con-

tagion. There was, he claimed, a "miasm" in the hospitals, which had become "foci of emanations" (*foyers d'emanations*).³²

In this fog of confused and *a priori* thinking, the contributions of Pacini and Snow were rays of light to which their contemporaries remained obstinately blind. With the death of Snow in 1858, Pacini was at the time of the third International Sanitary Conference alone in seeing clearly not only into the etiology of cholera but also into its pathodynamics. In 1865 he reiterated his views in a publication entitled "On the Specific Cause of Asiatic Cholera", in which he refers to the organisms that he had previously called "vibrios" as "molecules" (*molecole*).³³ Pacini had continued his painstaking microscopical observations both on the vibrios and on the epithelial lining of the small intestine.

Now if these infiltrated molecules multiply independently of the life of the individual that carries them, it is evident that they are *living beings* comparable to a *ferment*: and, as we shall see, it is the destruction that they produce in the *most superficial* part of the mucous membrane from which originate the *aqueous losses* by which cholera declares itself; therefore it is obvious that these molecules are the *original and specific cause* of cholera, and hence that they merit the name the *choleric ferment*.

The effect of these living organisms on the intestine, said Pacini, was to produce not a *haemorrhage* but a *lymphorrhage*, and the "*proximate cause*" of cholera was the "*loss of 3-4 pounds of water*" from the blood via the intestines. In a further publication³⁴ in 1866 he stated that the most probable mode of transmission of the "molecules" was that

they are propagated by means of *drinking-water*, or of foodstuffs, as are the germs of so many other *intestinal parasites*, when they pass from the body of one individual into that of another, without these individuals having had the slightest contact with each other, and remaining at a considerable *distance* from each other.

Pacini goes on to state that the development of the "*choleric ferment*" is incompatible with "good digestions", which can "digest also the cholera". He insists on the importance of dehydration in the disease, which "*drains the body*, reducing it almost to that of a mummy, unless death supervenes too soon", and he points out that the muscular cramps, shrivelled appearance of the skin, and the *vox choleric* all result from loss of interstitial fluid from the tissues which, instead of being irrigated by the blood-stream, are laid under contribution by it. Quantifying his concept of the pathological process in cholera, he estimated that the small intestine contained 4 million villi and that, allowing for

these, the total surface area of the alimentary tract, designated by the letter *S*, was 30 000 cm², of which the stomach accounted for 1000 cm², the small intestine 26 000 cm², and the large intestine 3000 cm².³⁵ When only a small portion of the small intestine was invaded by the cholera "molecules", a premonitory diarrhoea resulted, but once the critical area of 2000 cm²,³⁶ designated *s*, had been invaded, transudation from the affected mucosa equalled absorption by the unaffected area, *S-s*, and the threshold of the cholera process had been reached. Any area attacked in excess of *s* was designated *c*, the total area affected being *s + c* and the total healthy area *S - (s + c)*. At this point the volume of transudation exceeded the absorptive capacity of the unaffected intestinal mucosa, and unless the process ceased or could be arrested death from dehydration was inevitable. Using other alphabetical symbols for such factors as the volume of the rice-water stools, the amount of water lost from the blood, and the rates of intestinal transudation and absorption, Pacini developed equations to give algebraic expressions to the dynamics of the morbid process, describing them as the "mathematical laws" of cholera.

In 1867, the sixth International Statistical Conference was held in Florence, and the English Registrar-General, William Farr—one of the few contemporaries of John Snow to recognize the importance of his epidemiological investigations—was a participant. While in Florence, Farr visited Pacini's laboratory in the Hospital of Santa Maria Nuova. There he found Pacini, whom he describes as "one of the first microscopists in Italy", at work "examining the dejections and intestines of a young Danish artist who had just died of cholera". So impressed was Farr by Pacini's "mathematical laws" of cholera that, in the following year, he devoted to them nine closely printed pages of a Supplement to the Twenty-ninth Annual Report of the Registrar-General,³⁷ thus demonstrating both his scientific discrimination and his talents as a linguist. Farr points to the possibility of developing a similar mathematical approach to the prognosis of severe burns, and perhaps also of smallpox. But to most of Pacini's contemporaries, this explanation of the dynamics of cholera appeared to be over-simple.

³² Jaechnichen (1831) *Quelques réflexions sur le choléra-morbus*, Moscou.

³³ Pacini, F. (1865) *Sulla causa specifica del colera asiatico*, Firenze.

³⁴ Pacini, F. (1866) *Della natura del colera asiatico, sua teoria matematica e sua comparazione col colera europeo e con altri profluvii intestinali*, Firenze.

³⁵ Pacini later amended these estimates to 25 000, 1000, 20 000, and 4000, respectively.

³⁶ Later amended to 1000 cm².

³⁷ Farr, W. (1868) *Report on the cholera epidemic of 1866 in England. Supplement to the twenty-ninth annual report of the Registrar-General of Births, Deaths, and Marriages in England*, London.



National Library of Medicine, Bethesda, Md., USA

Although every medical student learns of pacinian corpuscles—microscopic bud-like terminals of sensory nerves in the skin that enhance the sense of touch—Filippo Pacini (1812–1883) of Florence, who described them, is one of the most neglected figures in the history of medical science. He anticipated by exactly 30 years Robert Koch's discovery of the cholera vibrio, and never ceased to insist that this organism was the cause of the disease. He died in the same year in which Koch sailed for Egypt, and later for Calcutta, as head of the German Cholera Commission. Thanks to Professor Rudolph Hugh of the United States, Pacini's discovery of the cholera pathogen received international recognition in 1965 when the Judicial Commission of the International Commission on Bacteriological Nomenclature decided that the preferred name of this microbe should be "*Vibrio cholerae* Pacini 1854". Pacini not only identified the cause of cholera as a specific germ but developed "mathematical laws" to explain its pathology, which were extraordinarily sophisticated for the time and correspond very closely with today's ideas. His brilliant researches and intuitions were so far in advance of his time that they made hardly any impact. His name was never even mentioned during any of the prolonged discussions of cholera at the International Sanitary Conferences. It is to the honour of William Farr that when he participated in the International Statistical Conference in Florence in 1867 he made a point of visiting Pacini at the hospital where he worked and found him "examining the dejections and intestines of a young Danish artist who had just died of cholera". Fascinated by Pacini's application of mathematical techniques to a disease process and describing him as "one of the first microscopists in Italy", Farr included in the 29th annual report of the Registrar-General of England an extremely detailed account of his "mathematical laws" of cholera. In 1871, Pacini expressed himself as "most amply compensated" by such recognition.

Pacini's incrimination of the vibrio as the cholera pathogen was to be repeated thirty years later by Robert Koch, and his explanation of the dynamics of the cholera process which, as he himself said, his Florentine colleagues had dubbed "in jest, but very justly", the *hydraulic doctrine*, was to be regarded as an entirely new concept almost one hundred years later.³⁸ Pacini expressed himself as "most amply compensated" by the attention that William Farr had given to his "mathematical laws" of cholera, but Farr's very detailed exposition made no more impact in England than had Pacini's original publications in Italy.

An awareness of the conflicting trends of thought about the nature of epidemic diseases at the time of, and shortly before, the third International Sanitary Conference is indispensable to the understanding of its discussions and to those of the next few conferences. The entirely different approaches of Pacini and Snow had shown the way, but the world was not ready for them, and both died some years before their ideas were finally vindicated.

The discussion at the conference

As soon as the initial procedural questions had been settled, the French delegation introduced an urgent proposal for the immediate appointment of a committee to consider the advisability of imposing a ban on all maritime communication between Arabian ports and the Egyptian littoral in the event that cholera should break out among the Mecca pilgrims, pointing out that in the previous year it was from Egypt that cholera had reached Europe via its Mediterranean ports. The conference, however, taken by surprise, decided to appoint a committee of seven to examine this proposal and another committee of nine to draw up a draft programme of work. Having completed its agenda for its first session, the conference then adjourned until 22 February.

At the second session of the conference, the chairman of the committee appointed to study the

³⁸ Pacini, F. (1817) *Sull'ultimo stadio del colera asiatico o stadio di morte apparente dei colerosi e sul modo di farli risorgere*, Firenze.

would be sufficient to change completely the relations of those Sovereigns with their subjects and would expose them to the attacks of a fanaticism all the more violent because in recent times everything had been done to restrain it. The European Powers could obtain everything from the peoples of Asia on condition that they knew how to save appearances and to give to their demands a form that would make them acceptable, and it was for that reason that the ports of Yambo³⁹ and Omar should be left open.

Other speakers against the proposal emphasized the gravity of the predicament in which pilgrims would find themselves if they were prevented from returning by sea. Mecca would not be able to provide food and drink for many thousands of them, forced to stay there until the cholera had subsided. If those wishing to return to or via Egypt had to go by land, where would they find the necessary provisions and camels to enable them to complete the long trek across the desert? If those wishing to return to India and beyond arrived at the port of Jidda to find their departure blocked and themselves destitute, would they not pillage the town? To these objections, Fauvel of France provided a lengthy refutation, arguing unconvincingly, on the basis of reports of an earlier Swiss traveller, Burkhardt, that ample material resources were available. Mirza Malkom Khan, he said sarcastically, had declared that Asian logic was different from European logic. "That was not necessary. We had already fully appreciated it." In his turn, Bartoletti, the medical delegate of Turkey, demolished Fauvel's contentions. Everything had changed since regular steam navigation had reached the Red Sea. The large numbers of camels that had constituted the means of transport for the lengthy desert crossings by caravan of yester-year were no longer available, and wells on the route had fallen into disrepair. Burkhardt had been to Mecca in 1814 and died in 1817. But since then all had been changed by steam navigation. To apply Burkhardt's experiences to contemporary conditions was tantamount to talking of travelling from Madrid to Paris by stagecoach.

Bartoletti's arguments were very compelling, and evidently based on very thorough personal knowledge, but after a debate lasting for three sessions the conference voted for the French proposal by 17 for, 8 against, and one abstention. Those in favour included each of the two delegates of France, Italy, Netherlands, Portugal, Prussia, Spain, and Sweden/Norway, the single delegate of Belgium, the medical delegate of Austria, and the diplomatic delegate of Greece (the Greek medical delegate being absent). The Austrian diplomatic delegate abstained, and no representative either of Denmark or the Papal States was present.

Against the motion voted both delegates of each of the four powers that Lenz of Russia had designated as being the most interested in the Mecca pilgrimage—Great Britain, Persia, Russia, and Turkey. Thus was a majority decision reached, early during the conference, at its fifth session on 1 March, on what might have been an important practical measure—the prohibition of all maritime communications between Arab ports and Egypt in the event that cholera should break out among the pilgrims, those pilgrims who wished to do so being left free to undertake the arduous overland journey to Egypt by caravan. That this was not an important measure resulted from the fact that none of the conference participants was bound by its decisions.

But this was not the only theoretically important decision reached. The conference was to hold 44 plenary meetings, the major result being agreement, often unanimous, on fundamental questions of principle.

Thus, it was agreed unanimously, with no abstentions, that:

Asiatic cholera, which on various occasions has travelled throughout the world, has its origin in India, where it arises and where it exists in a permanent endemic state.

There was similar unanimous agreement that it was unlikely that cholera would ever become endemic in Europe; that, in India, it was endemic principally in the valley of the Ganges; that, in India, pilgrimages were the most important cause of the development of epidemics; that the transmissibility of cholera was "an incontestable truth, proved by facts that admit of no other interpretation"; that man was the principal agent in the dissemination of cholera and a single case could give rise to an epidemic; and that maritime communications were the most important means of the distant spread of cholera, followed by railways. The last-mentioned conclusion needs qualification, for while cholera was imported into the Middle East by seaborne pilgrims, invasions of Europe before 1865 had spread overland.

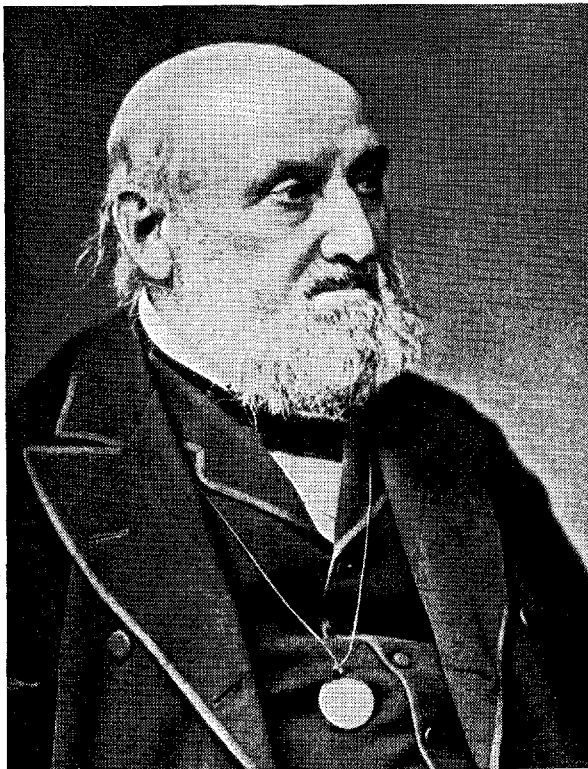
These major conclusions were based entirely on epidemiological considerations, and it is remarkable that an intergovernmental conference should have been able to agree unanimously to them at a time when there was a powerful body of medical opinion to which they would have been anathema. In fact, at one point a delegate expressed the fear that the wording of a resolution of "this all-contagionist conference" might be misinterpreted by "the anti-contagionists" as being favourable to the doctrine of the latter.

³⁹ Yambo, about 200 km west of Medina, is now called in *The Times atlas of the world* "Yanbu 'al Bahr". "Omar" is not to be found either in this atlas or in Lippincott's *Gazetteer*.

French proposal, Stuart of Great Britain, announced that his committee had not been able to agree on a report. He moved that the discussion should be adjourned *sine die*, on the ground that the proposal was based on an assumption that cholera was transmissible, while this was one of the main questions that the conference had been convened to study. It was only after this question had been settled that protective measures should be considered, and the French proposal was an invitation to the conference to start its work at the end. His task, said Stuart, was to oppose any measure that would interfere with trade unless its necessity could be proved. Gomez of Portugal, Krause and Mühlig of Prussia, and Monlau of Spain urged, on the contrary, that the conference should proceed to an immediate discussion of the French proposal in plenary session, upon which Lenz of Russia pointed out that the four powers most interested—Great Britain, Persia, Russia, and Turkey—favoured adjournment. This drew a strong protest from Sulpice-Antoine Fauvel of France, who stated that all powers represented at

the conference had the same interest as the four cited, whereupon Lenz explained that he had enumerated the powers that provided the greatest numbers of Mecca pilgrims. The chairman then put the matter to the vote, and it was decided by a majority of two that the French proposal would be discussed at the next session on the basis of a report by the committee of seven, Stuart requesting that the abstentions of the British delegates should be recorded in the minutes. However, when the committee's report was presented it proved to be of little help, since three members had voted for the French proposal and three against, with Stuart, its chairman, abstaining. During the debate on the report in plenary session, the Persian diplomatic delegate, Mirza Malkom Khan, claimed that acceptance of the French proposal

would raise storms of hatred in the Moslem world and create the most serious difficulties for oriental governments. The ideas, customs, doctrines and logic of Asia were so different from those of Europe that the mere idea that Moslem Sovereigns had come to an understanding with European Powers to regulate the progression of the pilgrims



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In 1837, the year of the accession of Queen Victoria to the throne, England inaugurated the systematic registration of births, deaths, and marriages, and appointed its first Registrar-General. Two years later Dr William Farr (1807-1883) was appointed to the General Register Office as "Compiler of Abstracts". Farr devoted the next 40 years of his life to the development and exploitation of a system of vital and health statistics. In his first report he wrote: "Each disease has, in many cases, been denoted by three or four terms, and each term has been applied to as many different diseases; vague inconvenient names have been employed, or complications have been registered instead of primary diseases. The nomenclature is of as much importance in this department of inquiry as weights and measures in the physical sciences, and should be settled without delay." In 1852 Farr published a monumental statistical report on a cholera epidemic in 1848-49 in England which took a toll of 53 293 lives of a total population of 17 million. The same pandemic cost an estimated 880 000 lives in Russia. Farr's report was described by the *Lancet* (1852, 1, 268) as "one of the most remarkable productions of type and pen in any age and country". He made similar reports on the cholera epidemics of 1853-54 and 1865-66, the latter being the last invasion of England by the disease. He was an ardent believer in the importance of securing international comparability of health statistics, and took an active part in the International Statistical Congresses held successively between 1853 and 1876 in Brussels, Paris, Vienna, London, Berlin, Florence, The Hague, St Petersburg, and Budapest. Farr has every claim to be regarded as the spiritual father of WHO's continuing activities in the development of the International Classification of Diseases, and the tenets that he proclaimed in his first report are as valid today as when he committed them to paper. He did not participate in any of the International Sanitary Conferences, but officially represented his government at most of the International Statistical Congresses.

The conference also voted unanimously that cholera was not endemic in the Hejaz⁴⁰ and was always imported from outside, but both British medical delegates and the medical delegate of Spain abstained from this vote, the British maintaining that cholera was already present in the Hejaz late in 1864 before the pilgrimage of 1865 had started. This was not the only occasion on which the British delegates showed some resistance to the idea that cholera was invariably exported from India, usually by steamships flying the British flag. A similar sensitivity was shown to a proposal, which was defeated by a large majority, that an international scientific commission should be sent to study cholera in its natural home, the British delegation declaring that this would constitute an infringement of the sovereignty of governments with possessions in India. Nevertheless, the British tacitly accepted that they had a special responsibility in regard to the spread of cholera from India, and presented a summary of sanitary improvements undertaken in Calcutta, Bombay, and Madras. Among these was the prohibition of the Hindu custom of throwing corpses into the Hooghly River. Instead, it was required that the bodies should be burned, and for this purpose a benevolent Calcutta Municipality provided free firewood to indigent relatives. Another administrative measure was the Native Passenger Act, which laid down minimum standards of accommodation and hygiene for British ships conveying pilgrims. While other delegates applauded these measures, one of them pointed out that pilgrim ships flying the Turkish or Arab flags were subject to no controls. Pilgrims were packed into ships of European construction that had been condemned as unseaworthy. The stench from these ships in port was sometimes so bad that neighbouring vessels were obliged to weigh anchor and move to windward of them. The wonder, he said, was that a single one of them reached its destination. The conference concluded unanimously, with some reservations by the British delegation, that the provisions of the Native Passenger Act, with some improvements as to sanitary precautions, should be made to apply to pilgrim ships flying any flag and coming from any country. It was also agreed by a large majority, only the two British and one of the Russian delegates voting against and the two Dutch delegates abstaining, that an internationally constituted sanitary commission should be established at the entry to the Red Sea at Suez.

The work of the committees

To facilitate its work, the conference had established special committees to report on: the origin,

endemicity, transmissibility, and propagation of cholera; specific preservation measures; general hygienic measures; measures to be taken in the Orient; quarantine; and the course of the 1865 epidemic.

Of these committees, by far the most important as reflecting scientific ideas of the time on cholera was the first-mentioned, which, for brevity, will be referred to below as the scientific committee. Several delegates had argued that it should be composed entirely of physicians, but after some discussion it was agreed as a compromise that it should consist of the diplomatic delegates of Belgium, France, and Spain, and all the 21 physicians participating in the conference, including the observer from Egypt.

A crucial question considered by the scientific committee was whether any precise conclusions could be drawn as to the nature of the generative principle (*principe générateur*) of cholera. On this point the committee agreed that:

Whether the generative principle of cholera be called a contagion, a germ, or a miasm; whether it be supposed that it be formed of an organized substance or not, it has always escaped all investigations, it has never been possible to isolate⁴¹ it, and it is known only by its effects. In this respect, it does not differ from other morbid principles. All that is known is that it regenerates itself in man in virtue of the morbid process that it has occasioned.

The committee concluded that in the present state of science it was not possible to do more than formulate hypotheses as to the nature of the generative principle. All that was known was that it originated in certain parts of India where it existed permanently, that it regenerated itself in man and accompanied him in his peregrinations, and that it could thus be propagated from country to country without ever reproducing itself spontaneously outside man. These conclusions were endorsed unanimously by the conference in plenary session, only Dr Goodeve of Great Britain abstaining.⁴² In its report, the committee cites Pettenkofer, Hirsch, and Griesinger as having demonstrated that a person coming from an infected area but suffering only from diarrhoea could import cholera into a healthy locality. This view was endorsed both by the committee and in a plenary session of the conference.

The conference also endorsed conclusions of the scientific committee that, in the light of present-day knowledge, seem paradoxical. Thus, it was concluded that the dejections of cholera patients were

⁴⁰ The holy land of Islam, including Mecca and Medina.

⁴¹ Obviously not in the modern sense of isolation by culture, but rather to "find" or "discover" it.

⁴² If not a total abstainer at the conference, Dr Goodeve came near to meriting such a designation.

"incontestably the principal receptacle of the morbid agent"; that anything contaminated by these dejections could also contain the generative principle; and that the genesis of the "choleric germ" took place "very probably in the digestive tract, perhaps to the exclusion of any other system of the body". All these conclusions would seem to point to oral ingestion of faecally contaminated matter as the mode of infection and contaminated water or foodstuffs as the most important vehicles. Yet the committee and the full conference concluded unanimously, with one abstention, that air was the main vehicle of the generative principle, although the disease could not be thus transmitted, "in the immense majority of cases", for more than small distances (Goodeve expressing a reservation only on this last point). The conference agreed that water could also be the vehicle, but voted unanimously, with neither abstentions nor reservations, that "the routes by which the toxic agent penetrates into the economy are principally the respiratory tract and very probably also the digestive tract". Only the preoccupation with the idea of aerial transmission and the spell cast by Pettenkofer's hypotheses could have produced such paradoxical results. For, in the discussions of scientific questions, the name of Pettenkofer was very much to the fore. In its report, the scientific committee had stated:

Water would seem, according to the observations made principally in England by Dr Snow, and in Germany by Dr Pettenkofer, to contribute, in certain circumstances, to the development of cholera in a locality.

In the previous paragraph of the report it had been asserted that it was "above all confined air" that served as the vehicle of the choleric principle. After some further references to Snow's observations in London, the report continues:

Although it is not the business of the conference to concern itself with theories, the doctrine of Mr Pettenkofer is so widely accepted, and relevant to factors so important for prophylaxis, that it is not permissible for us to disregard it. It rests on the generally admitted proposition that the intestinal dejections of cholera patients contain, at a certain stage, the propagating principle of the disease. This proposition, already formulated in 1849 by Dr Pellarin⁴³ (*Gazette médicale de Paris*), who insisted even then on the necessity for disinfecting the dejections of cholera patients with iron sulfate, was corroborated by the observations of Budd, published in 1854,⁴⁴ and by those of Snow; and then, it can be said, effectively placed beyond doubt by the researches of Dr Pettenkofer. . . . Mr Pettenkofer goes much further: he considers it to be proved by his observations that, in an epidemic of cholera, the soil itself of the area in which the disease prevails plays an important role in its development by the emanations that escape from it. It is thus that he believes that a porous soil, easily permeable to air and water

(and hence above all an alluvial or marshy soil), by becoming impregnated with excrementitious matter becomes first a receptacle and then, according to the circumstances, a more or less active focus from which the principle of the disease escapes. He maintains that the intensity of this escape of choleric matter depends on the level of the ground-water, and is consequently related to major or minor variations in the humidity of the superficial stratum of the soil.

This summary of Pettenkofer's doctrine was criticized at the 21st plenary session of the conference both by Pelikan of Russia and Mühlig of Prussia, who found it incomplete. Mühlig pointed out that the essence of Pettenkofer's doctrine was that two conditions were necessary for the development of cholera: (1) importation of the cholera germ into a locality; (2) a soil of particular constitution. Neither the first nor the second of these elements could alone produce the disease. The simultaneous action of both was required. The cholera patient supplied the germ, and the soil certain emanations, and the combination of these two, either in the environment or in the organism, resulted in the disease.

This elaboration of Pettenkofer's theory was endorsed by Pelikan and Lenz of Russia, Lallemand of France, and Salem of Egypt, the last having been Pettenkofer's pupil. Polak of Austria then read an article published by Pettenkofer in the *Zeitschrift für Biologie*⁴⁵ in 1865 (the content of this article has been summarized earlier). Maccas of Greece then stated that he supported the committee's report, while recognizing that it did not wholly reproduce Pettenkofer's doctrine. Goodeve of Great Britain and Bykow of Russia pointed out that nothing in the report was contrary to Pettenkofer's theory, and in this view they were followed by Fauvel of France. Monlau of Spain supported the report but, striking a rather anachronistic note, regretted that it contained no reference to the emotion of fear in the etiology of cholera. Maccas then denied that Pellarin was entitled to credit for advocating the disinfection of intestinal dejections. This was properly due to Professor F. Gietyl of Munich, who had as early as 1831 made reports to his government which resulted in an ordinance of 22 October 1836 requiring that dejections of cholera patients should "always and immediately be neutralized". In the event, Mühlig's further elaboration of Pettenkofer's doctrine was repro-

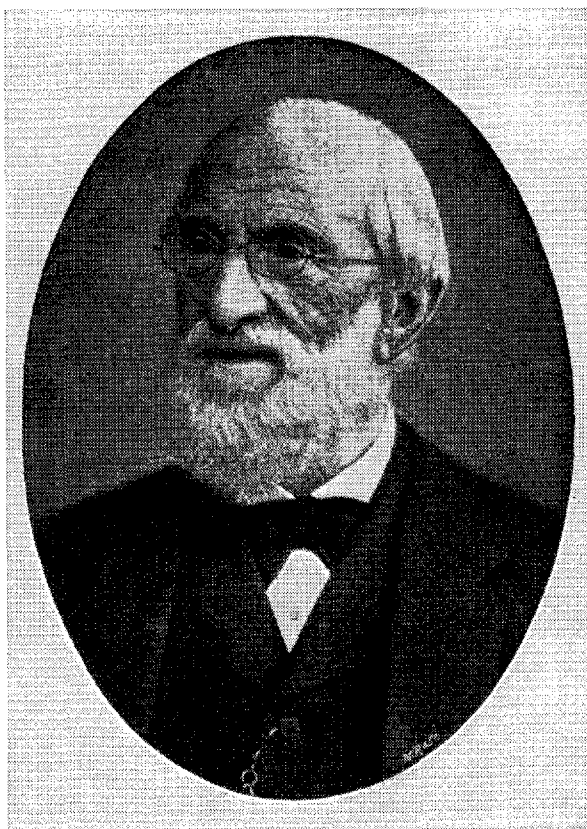
⁴³ It is true that Pellarin recommended chemical disinfection of cholera dejecta and latrines, but this reference to him is quite out of place. He thought that cholera was "an intoxication produced by the absorption of one or several deleterious gases emanating from decomposing animal matter, especially that contained in latrines" (*Gaz. méd. Paris*, 1849, 20, 991).

⁴⁴ Budd's publication was in 1849, not in 1854.

⁴⁵ Referred to as the *Journal de Biologie*, année 1665! The *Zeitschrift* was started by Pettenkofer largely as a vehicle for his doctrines.

August Hirsch (1817–1892) was, with Max von Pettenkofer, one of the German delegates to the fourth International Sanitary Conference in Vienna in 1874. It was at this conference that the first proposal was made for a permanent international health bureau, the principal function of which would have been to centralize epidemiological reporting internationally. But the time was not ripe for such a proposal, and it came to nothing. For all the delegates at the conference, the etiology and the mode of spread of the major epidemic diseases were still an enigma, and the utility of an international epidemiological bureau was far from obvious. It was to be another ten years before Robert Koch in Calcutta incriminated his “comma bacillus” as the pathogen of cholera, ten years more before Alexandre Yersin was to isolate the plague bacillus in Hong-Kong, and another six years before an American Army Commission was to prove in Cuba that yellow fever was transmitted to man by a mosquito.

Hirsch is best known for his massive handbook of “historical-geographical pathology” (*Handbuch der historisch-geographischen Pathologie*, 2nd ed., 3 vol. 1881–1886), which records the spread of epidemic diseases through the ages. An English translation of this was published by a famous English epidemiologist, Charles Creighton, in 1883–1886. In a letter to Creighton, Hirsch said that he had left a large part of his life in this work, which remains to this day a monument of scholarship. Hirsch was also the chief editor of the world’s most important collective medical biography—*Biographisches Lexicon der hervorragenden Ärzte aller Zeiten und Völker*, 6 vol., 1884–1888—and wrote histories of ophthalmology and of German medical science.



By courtesy of “The Wellcome Trustees”

duced as a footnote to the committee’s published report.

The attention given to Pettenkofer’s doctrine and the time devoted to discussion of it show that he dominated the scientific thinking of the conference. It was otherwise with Snow: apart from a brief reference to his views on the role of water as a vehicle of infection, the only other mention of his name in 1130 pages of conference proceedings is in the form of a protest by Lenz of Russia about its being coupled with that of Pettenkofer:

Pettenkofer repeated in Munich the researches of Snow in London but, as he has himself declared, without arriving at any result that could come to the support of the theory of Mr Snow.

In the entire record of the debates of this seven-month conference, there is no reference either to Hassall’s “myriads of vibriones” or Pacini’s “miriadi di vibrioni”.

Other decisions with scientific implications made by the conference were that the incubation period of cholera was not longer than a few days: for, 20;

against, 1 (Salem, Egypt); abstentions, 3 (Millingen, Netherlands; Mirza Malkom and Sawas, Persia). That no case was known of transmission by living animals: *unanimous*. But that it would be “rational” to regard them as “susceptible” in some cases: for, 16; against, 8 (both delegates of Great Britain, Netherlands, and Russia; Stenersen, Sweden/Norway; Salem, Egypt). That clothes and linen could be fomites: for, 21; against, 2 (Dickson, Great Britain; Stenersen, Sweden/Norway); abstentions, 2 (Keun, Netherlands; and Lenz, Russia). That merchandise could carry the disease: for, 16; against, 5 (Polak, Austria; Goodeve, Great Britain; Lenz and Bykow, Russia; Stenersen, Sweden/Norway); abstentions, 3 (van Geuns, Netherlands; Mirza Malkom, Persia; Hübsch, Sweden/Norway). It is to be noted that, in the cases of Austria and Great Britain, one of the two delegates voted for the motion and the other against, thus depriving their countries of any voice in the matter. Sweden/Norway also had a split vote, one delegate voting against and the other abstaining.

The conclusion that all arrivals from infected regions should be suspect obtained poor support, 14 delegates voting for and 10 abstaining, but there was a unanimous vote, with the abstention of Sawas of Persia, that although the infectiveness of the cadavers of cholera victims was unproven, they should nevertheless be considered dangerous. It was also agreed unanimously that soil impregnated with the dejections of cholera patients could for quite a long time retain the property of releasing the active principle of the disease, thus giving rise to an epidemic, and that disinfection was a "powerful auxiliary" in preventing or containing cholera.

The third International Sanitary Conference was in many respects a landmark. It had concentrated on one burning question: What were the appropriate measures to oppose to the murderous waves of cholera that had swept over the world from time to time since 1830? Agreement was reached that

India was the home of the disease, and that it was always exported from there by man. The painstaking investigations of Snow were brushed aside, and those of Pacini completely disregarded. Pettenkofer's theories—as elaborate as they were misguided—were treated with much respect, and were doubtless responsible to a large extent for the agreement that air was the principal vehicle for the transmission of cholera.

But these agreements were only on the surface, and were not to prove durable. Almost two decades later, at the sixth International Sanitary Conference in 1885, British delegates were to deprecate with an almost religious fervour the idea that cholera could be exported from India. The paradox is that, while their scientific thinking was hopelessly anachronistic, the measures that they advocated and adopted were completely in line with present practices.

The fourth conference: Vienna, 1874

As the second International Conference had been based largely on an analysis of the work of the first, so was the fourth essentially a review of the conclusions of the third. According to the *Lancet*, which carried full reports of the conference, Russia had taken the initiative in proposing to the other powers that the conference should be convened, in the hope of obtaining some relief from vexatious maritime quarantine requirements, as "practically the whole shipping trade of Russia passing through the Bosphorous has, since 1866, been at the command of the quarantine agents of the Porte⁴⁶ and their fancies."⁴⁷

In the eight years that had elapsed since the previous conference, both Pacini and Pettenkofer had continued to refine and consolidate their respective theories, neither paying in their writings the least attention to the views of the other. Pacini's contentions were based on patient and direct microscopical and clinical observations, Pettenkofer's on a tissue of indirect and circumstantial elements woven to support his preconceived theories.

In 1871, Pacini repeated his conclusions on the pathology of cholera in the following words:

Since my microscopic researches for the first time discovered the *choleric ferment* . . . ferment that, destroying the *absorbent epithelium* of the gastro-intestinal tube, transforms part of its *absorbent surface* into a *transudating surface*, it had become easy to understand how this last surface originates the *discharge* that first constitutes the *premonitory diarrhoea*, and later the *dejections of cholera*.

He then went on to summarize his formulation of the dynamics of dehydration in cholera, adding that in his own country it had encountered only "*a sardonic smile of compassion*".⁴⁸ A paradoxical observation made by Pacini, and by others before and after him, was that in fatal cases of cholera in which dehydration was so extreme as to produce almost a state of mummification the cerebrospinal fluid was copious. Pacini attributed this phenomenon to the combined effects of atmospheric pressure and the incompressibility of the bony housing of the fluid, and in this he found—rightly or wrongly—an explanation for the mental lucidity that he and earlier observers had noted even in the terminal stages of the disease.

As for the treatment of cholera, Pacini had earlier strongly opposed intravenous infusion. This method had first been tried in Moscow in 1830, and further developed in Scotland, but with the crude apparatus of the time and the lack of aseptic precautions patients often died rapidly from air embolism or more slowly from septicaemia. Pacini believed that it was not justifiable to employ such a perilous treatment except in the "*stage of apparent death*", in which case it was "*the sole remedy that remains to be tried*". He recommended a solution of 10 grams of sodium chloride in a kilogram of water, and stated that if the "*cadaver*" had not been resurrected after the injection of this volume of fluid it was useless to continue.

In Germany, the great Rudolf Virchow had two years before expressed scepticism about the importance of ground-water in the etiology of cholera. Pettenkofer was not slow to react. In the same year he published in the *Zeitschrift für Biologie* a wordy (140-page) article on "soil and ground-water in their relation to cholera and typhoid", which was reprinted as a separate monograph.⁴⁹ In England, he says, striking facts have been demonstrated and become known, which have not only deeply shaken "the one-and-only drinking-water faith", but in the majority of cases rendered it "downright impossible." He quotes (in English) a "Mr Jabez H. Ogg"⁵⁰ as saying that "the water theory would no longer hold water". Pettenkofer then concretizes his own hypothesis in the following terms: The specific cholera germ (*Cholerakeim*) from India can be designated *x*; the substrate, which is linked to locality and season (*Ort und Zeit*), *y*; and the product of both of them—the real cholera poison (*eigentliche Choleragift*)—as *z*. "Neither *x* nor *y* can alone originate cholera, but only *z*." At present, he adds, the nature of *x*, *y*, and *z* is unknown, but it is probable that all three are organic and that at least *x* is an organized germ

⁴⁶ Turkey.

⁴⁷ *Lancet*, 1874, 2, 20.

⁴⁸ Pacini, F. (1871) *Sull'ultimo stadio del colera asiatico o stadio di morte apparente dei colerosi e sul modo di farli risorgere*, Firenze.

⁴⁹ Pettenkofer, M. von (1869) *Boden und Grundwasser in ihren Beziehungen zu Cholera und Typhus*, München.

⁵⁰ The name was in fact "Hogg".

(*Keim*) or body. In the human intestine, *x* can nourish itself and perhaps even multiply, but in a case of cholera the human body is only the theatre for the operations of *z*, and can never itself produce *z* except in the presence of *y*.

It is difficult to imagine a more flagrant disregard of Occam's razor—*entia non sunt multiplicanda praeter necessitatem*—than Pettenkofer's triad of causes of cholera. But for three decades more he was to persist in his theories, until in 1901 he finally removed himself, but not his disciples, from the scene by blowing out his brains. As has been seen, Pettenkofer's far-fetched doctrine had been a *Leitmotiv* of the third International Sanitary Conference, and it was to continue to befog ideas on the nature of cholera for many years.

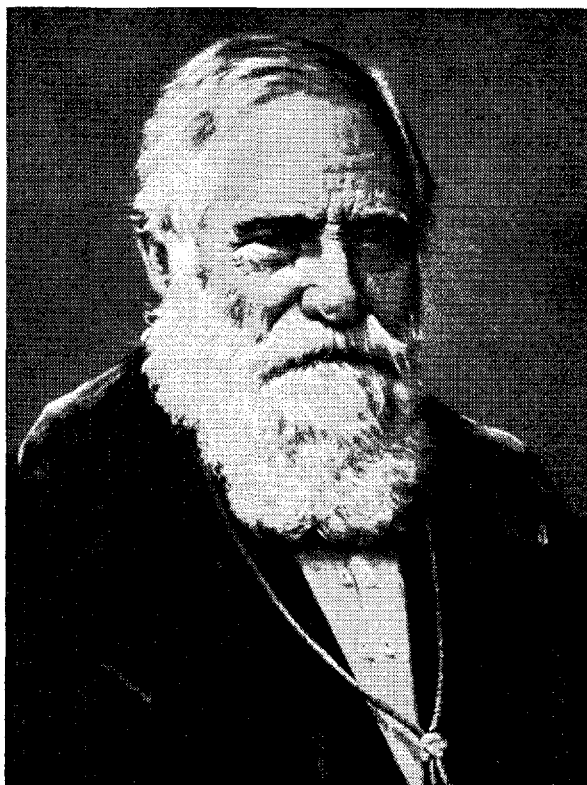
In Britain, Pettenkofer's theories seem to have had little impact on the public health authorities. In a memorandum published on 5 July 1873 over the signature of its Medical Officer, John Simon, the Local Government Board pointed to the existence of cholera in continental Europe and stressed the vital importance of an uncontaminated supply of drinking-water in avoiding an outbreak of the

disease in England.⁵¹ The heavy responsibility of the water-companies for the lives of hundreds if not thousands of their customers was also emphasized, and Simon warned that:

It is characteristic of cholera (and as much so of the slightest choleraic diarrhoea as of the disease in its more developed and alarming forms) that *all matters which the patient discharges from his stomach and bowels are infective*. Probably, under ordinary circumstances, the patient has no power of infecting other persons except by means of these discharges; nor any power of infecting even by them, except in so far as particles of them are enabled to taint the food, water, or air, which people consume.

Simon points to the danger of contamination of wells by seepage from cesspools and drains, and adds that even a single case of cholera of the slightest degree may "exert a terribly infective power on considerable masses of population". There are, says Simon, two main dangers: first, the contamination of water-supplies by "house-refuse or other like kinds of filth"; second, "breathing

⁵¹ Simon, J. (1874) In: Great Britain, Privy Council, *Reports of the Medical Officer of the Privy Council and Local Government Board, New Series, No. 1*, London.



Max von Pettenkofer (1818–1901) was one of the German delegates at the fourth International Sanitary Conference in Vienna in 1874. He was a pioneer of environmental health, making important contributions to the hygiene of housing, to the sanitary disposal of human wastes, and to the provision of pure water supplies. In addition he made significant biochemical discoveries, invented a system for lighting by wood gas, improved methods for the assay of precious metals, and even devised a method for restoring ancient paintings. In his younger days Pettenkofer was for a short time an actor, and this early experience left its mark in the form of a rather flamboyant personality. His Achilles heel was his famous *Bodentheorie* (soil theory). For almost half a century he persistently and obstinately ridiculed what he called the "drinking-water theory" of the transmission of diseases that are typically waterborne—such as cholera and typhoid. He once wrote that if cholera were conveyed by drinking-water it would be "childishly simple" to prevent it. According to Pettenkofer, cholera was caused by a factor, *x*, which combined with something in the soil designated as *y* to form *z*. The last of these was "the real cholera poison". When Robert Koch incriminated the cholera vibrio as the pathogen, Pettenkofer agreed that it was *x*, but insisted that it was harmless without *y* and *z*. To prove his contention, in 1892 he swallowed a pure culture of cholera vibrios, histrionically comparing himself to "a soldier on the field of honour". As a result, Pettenkofer suffered mild digestive disturbances, but this was a meaningless autoexperiment, for if a hundred people were to repeat it simultaneously a few would contract cholera and the majority would not. Pettenkofer had a large following in many countries. In 1901, at the age of 83, he committed suicide.

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air which is foul from the same sorts of impurity". There is no hint of Pettenkofer's alphabetical entities *x*, *y*, and *z*, nor of Pacini's "molecules", and the idea of specificity of the cause of cholera is lacking, for Simon appears to believe any kind of "filth" to be a hazard, as also foul air.

But Pettenkofer's ideas found a readier reception in traditionally anti-contagionist British India, and D. D. Cunningham, an Army surgeon attached to the Sanitary Commissioner with the Government of India, stated in an unpublished report on cholera dated 1871 that all experience of the 1870-71 cholera season in the Madras Presidency tended to confirm the truth of the "soil theory", as opposed to the "water theory" and the "contagion theory". Cunningham did not unreservedly embrace the "soil theory" but felt that, on balance, it accorded better with the observed facts than the others. Much of his report is taken up by accounts of numerous microscopical observations on water from tanks and wells in cholera-infected localities and on cholera dejecta. From these observations he concludes that there are neither specific "*Bacteria*" or "*Vibriones*" associated with cholera, nor a peculiar proliferation of any of the normal intestinal flora. Where microorganisms appear to be particularly numerous, this may, he thinks, be attributed to decomposition of the intestinal contents.

In France, the official Consultative Committee for Public Health had published a memorandum dated 25 September 1871 advising the public on preventive measures against cholera.⁵² The memorandum states that the generative principle of cholera is contained in the dejections of cholera patients and that it escapes after a certain time, on contact with air. The principle was able to maintain its activity in water, cesspools, drains, and even rivers, and to penetrate porous soil, remaining there in a latent state until, under certain conditions of heat and dryness, it escaped with more or less pernicious effects. The problems of the immunity of certain localities, such as the town of Lyons, and of certain individuals were as yet unsolved, but it was known that undue fatigue, drunkenness, and all other excesses were predisposing factors. As so often before, both in Europe and North America, fear was adduced as an "adjuvant cause of cholera", and those who were frightened were urged not to stay in areas affected by disease, lest their presence increased the number of victims to no purpose. The only echo of Pettenkofer's doctrine is the reference to porous soil. As protective measures, drinking-water should be protected against contamination from cemeteries, cesspools, and all organic matter, and should preferably be brought to its point of consumption without exposure to air or light.

Drunkenness should be punished to the extent that the law permitted. It was generally agreed that the cholera germ was the product of a sort of fermentation of the choleraic dejections that took place on contact with air, and that they should therefore be destroyed or neutralized as soon as possible.

Adrien Proust, long to be the leading French authority on questions of international hygiene,⁵³ was sympathetic to Pettenkofer's doctrine, but with some reservations.⁵⁴ In 1873 he summarized his attitude as:

without conceding to Pettenkofer's theory the absolute value attributed to it by its author and his compatriots, it is beyond doubt that porous, permeable, and damp soils provide the conditions most favourable for the propagation of cholera.

Proust was convinced that cholera was transmissible from man to man, and that:

The cholera miasm appears to be volatile; it mingles with the ambient air, which seems to be its principal vehicle, and retains all its activity in confined air.

However, he did not believe that air was the sole vehicle of the miasm. Water was "also an agent in the propagation of the disease". He refers at some length to Snow's observations, but twice qualifies Snow's emphasis on this mode of propagation as "exaggerated". He nowhere refers to the work of Pacini.

In 1873, Pettenkofer, together with the distinguished epidemiologist, August Hirsch, proposed to Chancellor Bismarck that a special committee of experts should be appointed to elaborate a plan of research on cholera. Thus came into being the Cholera Commission of the German Empire, consisting of five members, including both Pettenkofer and Hirsch.⁵⁵ At its first meeting on 4 August of the same year, the Commission elected Pettenkofer as its chairman. It decided that it would not confine itself exclusively to cholera, but would include "etiological subjects common to all epidemic diseases, such as typhoid, yellow fever, dysentery, etc.". These diseases, said the Commission, had an etiological bond that made the study of one of them equally applicable to the others, and here was a relic of the idea of the transmutability of communicable diseases. However, in view of the reappearance of cholera in Germany, the Commission felt obliged to start with discussions of

⁵² France, Comité consultatif d'Hygiène publique (1871) *Instruction générale concernant les mesures préventives à prendre contre le choléra*, Vienna (Text annexed to the proceedings of the International Sanitary Conference held in Vienna in 1874).

⁵³ And also the father of the more famous Marcel Proust.

⁵⁴ Proust, A. (1873) *Essai sur l'hygiène internationale*, Paris.

⁵⁵ *Plan de recherche pour l'étude de l'étiologie du choléra et de sa prophylaxie*, Vienna (Text annexed to the proceedings of the International Sanitary Conference held in Vienna in 1874).

measures that, "in all probability", had contributed to the prevention or retardation of the development of the disease. It recommended that the notification of all cases should be obligatory and that special printed forms should be provided for this purpose, for which the postage would be free. Man, it warned, was the most important agent for transmission of the disease, and the "cholera virus" could become attached to the person of a healthy man, who could transmit it without suffering any ill effects himself. Animals and inanimate objects could also be sources of infection, as could foodstuffs contaminated either by direct contact or by precipitation from the atmosphere. A supply of pure drinking-water was important, but no proof as yet existed that water could carry the cholera virus. The circumstances of each case should be investigated by reference to topographical features, dwellings, dress, diet, occupation, sanitation, water-supply, and many other elements—even including the material with which the patient's pillow was stuffed. The report contains few traces of Pettenkofer's doctrine, except for a certain preoccupation with the need for investigations of soil and ground-water.

This, then, was the contemporary medical background to the fourth International Sanitary Conference when it opened in Vienna on 1 July 1874. Twenty-one countries were represented, four of them—Luxembourg, Romania, Serbia, and Switzerland—for the first time.⁵⁶ This was the first of the International Sanitary Conferences to follow a relatively modern pattern, both in respect of its duration (for it lasted only a month)⁵⁷ and in adopting written rules of procedure (*règlement*) to regulate its debates. Moreover, these rules specified that each country, or each health administration,⁵⁸ should have only one vote, whatever the number of delegates it had sent. As a general rule, French was to be the language of debates and of the conference proceedings, although delegates could speak in another language if they so wished. The conference held 20 plenary sessions, and adjourned on 1 August.

The German delegates were Pettenkofer and Hirsch, while one of the three French delegates was A. Proust. Also participating in the conference was Bartoletti—now Bartoletti Effendi—representing Turkey, as he had done almost a quarter of a century before at the first International Sanitary Conference.

The main task of the conference was to examine the conclusions of the Constantinople conference of 1866 and decide to what extent they were still valid. It unanimously confirmed the conclusion that cholera originated only in India, and that

outbreaks in other countries were always imported from outside, Hirsch pointing out that it was indisputable that before 1817 all countries of the globe except India and Ceylon had been exempt from the disease. The question whether cholera was propagated by man was then put to the vote. At Constantinople there had been a unanimous affirmative vote, with Monlau of Spain abstaining. Again, the vote was unanimous, but this time it was Pettenkofer who abstained, declaring that the focus of cholera was a particular locality, whence man propagated the germ. Marcovitz of Romania stated that Pettenkofer's intervention, far from clarifying the question, led to a regrettable confusion. Four other delegates also spoke against Pettenkofer's reservation but the conference ultimately adopted unanimously a resolution that is incomprehensible as a whole, except in the light of Pettenkofer's theories:

The conference accepts the transmissibility of cholera by man coming from an infected environment; it considers man as able to be the specific cause only outside the influence of the infected locality; further, it regards him as the propagator of cholera when he comes from a place where the germ of the disease already exists.⁵⁹

The second of the three clauses appears to contradict the other two, but this apparent contradiction was merely a reflection of Pettenkofer's theory that one of the etiological elements, *x*, could be transported by man from place to place but was innocuous until it combined in a suitable soil with *y* to produce "the real cholera-poison", *z*. Thus, man could transport *x* from an infected to an uninfected locality, but once *x* had combined with *y* to produce *z* the role of man was no longer of any importance.

On the question whether cholera could be transmitted by foodstuffs, Semmola of Italy cited Thiersch's experiments on mice of almost 20 years before but made no mention of his compatriot Pacini. Thiersch, like Pettenkofer, a citizen of Munich and doubtless influenced by his ideas, had tried to produce experimental cholera in mice, starting from the assumption that the cholera principle had to undergo a certain decomposition

⁵⁶ The other seventeen were Austria-Hungary, Belgium, Denmark, Egypt, France, Great Britain, Germany, Greece, Italy, Norway, Netherlands, Persia, Portugal, Russia, Spain, Sweden, and Turkey.

⁵⁷ The annual World Health Assembly normally lasts for three weeks.

⁵⁸ The result of this curious provision was that Austria-Hungary had two votes—one for Austria and the other for Hungary. A modern parallel is to be found in the separate votes that Byelorussia and the Ukraine have in the United Nations.

⁵⁹ The original French text of this resolution reads as follows: "La conférence accepte la transmissibilité du choléra par l'homme venant d'un milieu infecté; elle ne considère l'homme comme pouvant être la cause spécifique, qu'en dehors de l'influence de la localité infectée; en outre, elle le regarde comme le propagateur du choléra, lorsqu'il vient d'un endroit où le germe de la maladie existe déjà."

before becoming infective. He kept specimens of the intestinal contents of fresh cholera cadavers or the rice-water stools of patients for periods ranging from one to 18 days, each day being a "decomposition day" (*Zersetzungstag*). He soaked separate pieces of filter-paper with each of the various vintages, dried them, and then fed them to mice. He claimed that of a total of 110 mice so treated, 47 contracted watery diarrhoea and 14 died with postmortem appearances similar to those seen in human cases of cholera. He referred to the pieces of filter-paper so processed as "preparations", and stated that only preparations made from dejecta in their 3rd to 15th "decomposition days" were active.⁶⁰ It is now known that mice are completely immune to cholera and that the cholera vibrio does not withstand drying for more than a few hours. But what is truly remarkable is that 11 years later, in 1867, an eminent British medical scientist, John Burdon Sanderson, claimed to have successfully repeated the experiments of Thiersch, using 50 mice.⁶¹ These experiments, he said,

clearly show that the liability to attack was greatest as regards the third and fourth days, much less and nearly equal as regards the second and fifth days, and least as regards the first day.

As will be seen later, almost 30 years after Thiersch's experiments, Robert Koch was to misunderstand them completely and to write that Thiersch had claimed to produce experimental cholera in mice "by feeding them with cholera intestine".⁶²

Conference participants did not make any appraisal of Thiersch's alleged findings, but after further discussion voted by 11 to 7 that they had not enough information to take a decision on the question, the dissidents being Austria, Hungary, Italy, Norway, Romania, and Switzerland. There was a unanimous vote, without discussion, that drinks, especially water, could propagate cholera, and a vote of 10 for to 2 (Persia and Serbia) against, with 6 abstentions (Belgium, Great Britain, Greece, Luxembourg, Netherlands, and Russia), that the possibility should be admitted of animals being able to transmit cholera to man. On the question whether goods could transmit the disease, 13 voted that the possibility must be admitted, while 5 (Belgium, Great Britain, Persia, Russia, and Serbia) abstained. The conference voted unanimously that "the ambient air is the principal vehicle of the generative agent of cholera", but that it quickly lost its activity in the presence of fresh air. In confined air, however, it could preserve its activity indefinitely. There then followed a lengthy discussion on the incubation period of cholera,

initiated by Pettenkofer's objection to the conclusion of the Constantinople conference that this was only a few days. Switzerland alone came to Pettenkofer's support and was the only delegation to vote against that conclusion, 13 other delegations voting for it and 4 (Germany, Luxembourg, Romania, and Sweden) abstaining. On the question whether disinfection measures were known that would destroy or attenuate the "generative or contagious principle" of cholera, the voting was strangely illogical. Twelve voted that this was *surely* the case and 7 abstained, while the voting whether there was *some chance of success* was 13 for and 5 (Austria, Hungary, Denmark, Germany, and Russia) against, only France abstaining. But the conference then voted unanimously on a compromise resolution that referred to "substances now regarded as disinfectant".

By the end of its fifth session on 6 July the conference had, in less than a week, made decisions on all the scientific questions before it. There remained for consideration two major administrative problems: the preparation of draft regulations for maritime quarantine, and the creation of a permanent international commission on epidemics which, in the words of the Austro-Hungarian Foreign Minister at the inaugural session of the conference, would

morally and materially encourage the noble devotion of those who would wish to dedicate themselves to the exclusive study of a scourge as mysterious in its origin as in its development.

To aid in the study of each of these problems committees were appointed, the first composed of Alber-Glaustätten (Austria), Hirsch (Germany), Seaton (Great Britain), Semmola (Italy), and van Cappelle (Netherlands), and the second of Catinelli (Austria), Kierulf (Norway), Lenz (Russia), Marcovitz (Romania), and Polak (Austria). The conference rejected land quarantine as "unworkable and consequently useless" by a majority of 13 to 4 (France, Greece, Portugal, and Serbia), with 2 abstentions (Luxembourg and Switzerland). As to maritime quarantine, the first report of the relevant committee was sharply criticized by Egypt, France, Greece, Portugal, Serbia, and Turkey, and the French moved that the committee should be asked to make a further report taking into account the "special conditions" of quarantine in "certain States of Southern Europe", and

⁶⁰ Thiersch, C. (1856) *Infektions-Versuche an Thieren mit dem Inhalte des Choleraadarmes*, München.

⁶¹ Sanderson, [J.] Burdon, "Report by . . . on the experimental proofs of the communicability of cholera." Appendix No. 9 to: Great Britain. Privy Council. *Ninth Report of the medical officer of the Privy Council*, 434-58, London, 1867.

⁶² *Dtsch. med. Wschr.*, 1883, 9, 615.

that additional members from these states should be co-opted. The French delegation had previously pointed out that the differences of opinion were largely between the Mediterranean countries, which favoured quarantine, and the northern countries, which did not, and that even within France itself there was a comparable divergence, the Mediterranean ports being for quarantine while those of the English Channel were against. A notable exception to this generalization was Italy, which formed part of the anti-quarantine faction. Put to the vote, the French motion was narrowly lost by 11 to 10. An Italian motion that the committee should revise its report without co-opting additional members was carried by 16 to 1 (Egypt), with 4 abstentions (France, Portugal, Serbia, and Turkey). The committee on quarantine had prepared its report in the form of a set of draft regulations providing that a rigorous medical inspection should replace quarantine. When it had amended the report to take account of objections, the conference considered and voted upon the draft, paragraph by paragraph. However, by the 14th meeting it had become obvious that there were irreconcilable differences in regard to the necessity of maritime quarantine, and Hirsch, pointing out that the "dualism" between those who favoured quarantine and those who wished to substitute a system of medical inspection could not be resolved by further discussion, proposed that both systems should be regarded as justified and that each state should be free to choose between them. It was nevertheless important, he said, that each system should be applied in a uniform fashion. He therefore proposed that, in addition to the committee on maritime quarantine that had recommended its abolition, another committee on the same subject should be appointed to elaborate international quarantine regulations. The conference agreed to this proposal and appointed a second committee consisting of three of the members of the first committee—Hirsch, Alber-Glaustätten, and Seaton—and two new members, Fauvel (France) and Bartoletti (Turkey). Finally, at its 16th meeting on 25 July the conference voted unanimously, with the abstention of the Spanish delegation—which had not put in an appearance at the conference before the previous session on 23 July—for a set of regulations that provided both for the abolition of maritime quarantine and for its retention, thus ensuring international harmony.

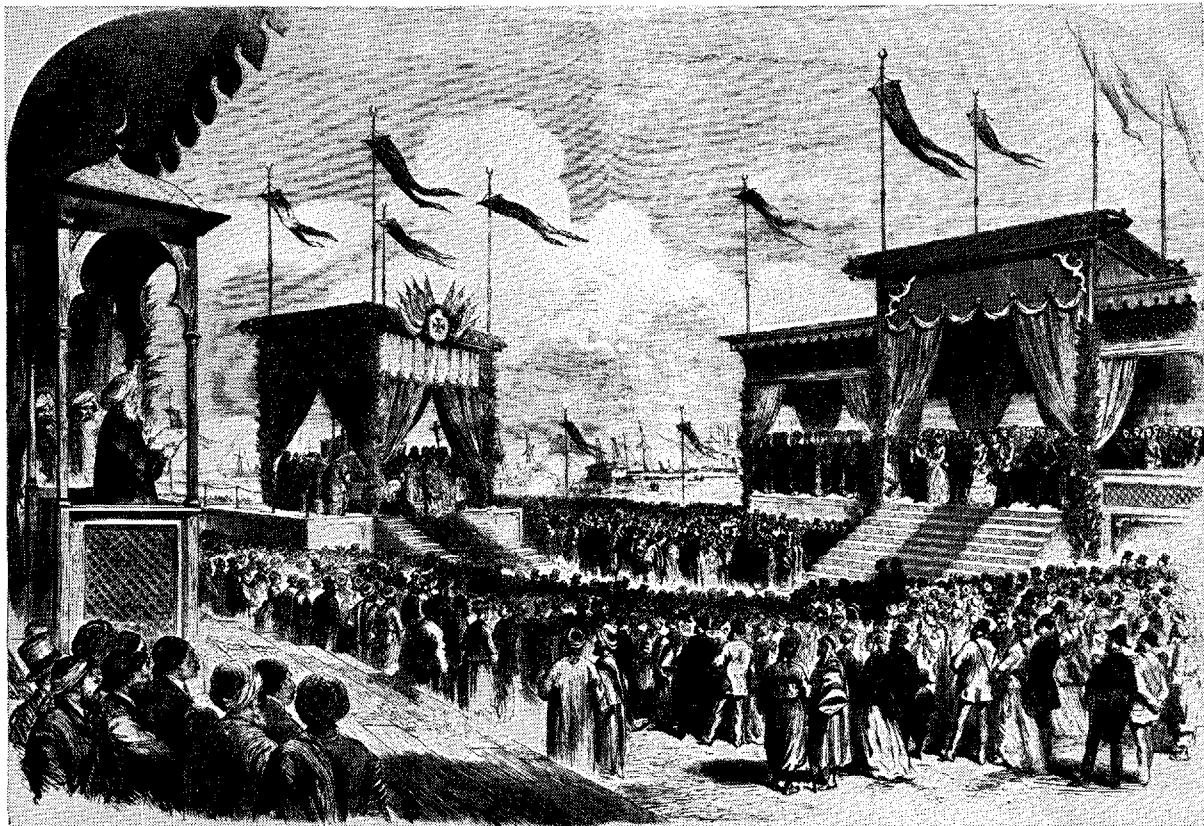
The next business to be considered was the report of the committee on the creation of an international sanitary office, which the committee had prepared in the form of proposed statutes for such an office. The conference unanimously⁶³

voted for these statutes, after some amendments to them, thus agreeing that there should be established in Vienna a "Permanent International Sanitary Commission having as its object the study of epidemic diseases". The responsibilities of the Commission would be "purely scientific", and it would have as its "principal task the study of cholera". Nevertheless, it could also study other epidemic diseases. The Commission was to be composed of medical delegates of participating governments and was to have a headquarters with a staff that the Commission would appoint. Annexed to the statutes was a summary of "first investigations" to be undertaken by the Commission, based on a paper submitted by Pettenkofer, in which he asserted, *inter alia*, that "the behaviour of cholera on ships speaks against the contagionist opinion, and much more clearly than on land". The investigations were to be: (i) regular and thorough study of the amount of rain and of evaporated water in eight named towns in Asia Minor and North Africa; (ii) study of the telluric conditions of those towns; (iii) a close analysis of the appearance and spread of cholera on ships; (iv) determination of the first cases of cholera, especially in the maritime ports of Europe, and compilation of a complete statistical account of the spread of cholera in Europe; (v) scientific study of the precise duration of the incubation period in cholera. The conference also expressed, in an "additional article", the desire to see established in Persia an International Health Council (*Conseil de Santé internationale*) similar to those that had operated "so advantageously" in Constantinople and Alexandria.

In the event, the Permanent International Sanitary Commission never materialized. As for the International Sanitary Council of Persia, it had nominally been created after the Constantinople conference, but was only "a sort of society of medicine and hygiene". It was not until thirty years later that it became an effective instrument, although remaining purely national in its constitution.

At the penultimate session of the conference, on 29 July, Portugal, Spain, and France contributed lengthy interventions on the subject of yellow fever. Pettenkofer then moved that the discussion be closed and that the question of yellow fever be referred to the Permanent International Sanitary Commission. In this motion he was supported by Marcovitz of Romania, who added the wish that America should participate in the work of the International Commission in view

⁶³ Great Britain was the sole abstainer in the vote on the first article of the statutes and withdrew from the meeting during the voting on the subsequent articles.



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This picture from the *Illustrated London News* gives a vivid idea of the sumptuous ceremony at Port Said that attended the opening of the Suez Canal in 1869, one of the greatest of the many great engineering achievements of the nineteenth century. The importance that European countries attributed to this short cut to the Indian Ocean was indicated by the presence of royal personages, including the Empress Eugénie of France. Five years later the fourth International Sanitary Conference was held in Vienna, and a curious feature of it was that the possible epidemiological significance of the Suez Canal was not even discussed. It was otherwise with the sixth conference in Rome in 1885 and the seventh in Venice in 1892, at both of which quarantine requirements for ships traversing the canal were the most hotly debated subject. The country most concerned was Great Britain, because of the intensive maritime traffic between it and India and beyond. The British strenuously maintained that their ships traversing the canal, having no contact with the land, and bound directly for British ports, offered no threat to continental Europe. Other countries claimed that before entering the canal the passengers and crew of infected or suspect westbound ships should disembark and remain in quarantine for five days. No agreement was reached at the Rome conference, but that at Venice seven years later resulted in the first international treaty relating to health. This was concerned solely with conditions for the transit of ships through the canal. In fact, in more than a century cholera was never brought to Europe by sea via the Suez Canal. As Robert Koch pointed out in 1894, the disease normally invaded Europe by land. He denounced lengthy international arguments about maritime quarantine as " quite superfluous ".

of its special experience of yellow fever. The conference endorsed Pettenkofer's motion. The closing session was held three days later, on 1 August, when all the delegates signed a final act summarizing the decisions reached—decisions that left all participating countries free to do whatever they would have done if the conference had never taken place. Pettenkofer had intervened very little in the debates,

and paradoxically, in spite of his personal participation, the influence of his doctrine was rather less in evidence than it had been during the Constantinople conference eight years before. A strange feature of the conference was that no reference was made to the opening of the Suez Canal five years earlier—an event that was surely of major epidemiological interest.

The fifth conference: Washington, 1881

In the seven years separating the fourth and the fifth international sanitary conferences, both Pacini and Pettenkofer continued to proclaim the doctrines that each had initiated in 1854 and 1855 respectively. Pettenkofer reiterated in 1878 his disbelief in—or, as he says, his “conviction of the non-influence” of—the role of drinking-water in cholera, claiming that he based himself not on “isolated facts but on a series of facts”.⁶⁴ He refers those wishing for a fuller exposition of his opinion of the “drinking-water theory” to a long paper that he had published four years before to disprove a connexion between drinking-water and typhoid. In a lecture delivered to the Munich medical society in 1880, he declared: “the more eagerly I applied myself to proving the influence of drinking-water on cholera and typhoid, in which I originally believed, the more untenable I found the hypotheses”.⁶⁵ He was, he said, in agreement with Dr J. Cunningham, Dr D. Cunningham, and Dr T. Lewis in India, who after unprejudiced and exact investigations had found no followers of the drinking-water theory in the homeland of cholera, and he again asserts that the cholera-producing organism, *x*, cannot propagate the disease without the substrate, *y*, which originates in the soil. Even when, as in the case of cholera outbreaks on ships, the soil was not a factor, *y* from the land must be present. Thus did Pettenkofer accommodate the facts in the Procrustean bed of his soil theory.

Pacini was equally tenacious in his views, an important difference between him and Pettenkofer being that he had derived correct conclusions from direct personal observation, while Pettenkofer was leading his followers in an epidemiological wild-goose chase based on nothing but an over-active imagination. Pacini again insisted in 1876 that the pathological changes in the intestine in cholera could be due only to the “*molecular ferment*” that infiltrated the mucous membrane, multiplied there, and was the “*specific cause*” of the disease.⁶⁶ Referring to the treatment of cholera, he repeats his earlier advice that once a patient has reached the “stage of apparent death”, the only therapeutic procedure that remains is the intravenous injection of a 1% aqueous solution of sodium chloride.

In 1879, Pacini published in the journal *Lo Sperimentale* a full account of his findings and conclusions on the nature of cholera, and in the following year, three years before his death, he brought out in book form a second and amplified edition of this.⁶⁷ He quotes with approbation the words of a French author, Jaccoud, who wrote in 1879:

the multiplicity of medications directed against cholera is due to ignorance of precise ideas of its pathogenesis. The strangest theories have produced the most bizarre treatments; that had to be, but it is no longer admissible; the indications furnished by the pathogenesis must, as always, be followed. However, the fundamental indication has already been formulated since 1830 by Hermann: ⁶⁸ it is necessary, above all, to arrest the intestinal discharge, in order to prevent thickening of the blood and the occurrence of asphyxia and inanition.

Pacini then insists that the primary cause of cholera is a contagion, which comes always from India, and the vehicles of which are water, raw foods, or the ambient air. The contagion is a “special species of *microbe*”, which acts “only locally” on the intestinal epithelium “without producing any general infection”, as is the case with the action on the skin of the acarus of scabies or the fungus of ringworm. When cholera is present in a country, he maintained, many people who had “*cholericogenic microbes*” in their intestines suffered only a mild diarrhoea, which produced no noticeable alteration in their state of health and left them able to go about their daily occupations. Such people could, by their excrements, spread cholera to a distant country “without being affected by it”.

In summary, Pacini identified the cholera vibrio and recognized that it was the pathogenic agent of the disease; that it acted locally on the intestinal mucosa; that its effect was the production of

⁶⁴ *Z. Biol.*, 1878, 14, 297.

⁶⁵ *Ärztliches Intelligenz-Blatt*, 1881, 28, 35, 47.

⁶⁶ Pacini, F. (1876) *Sopra il caso particolare de morte apparente del ultimo stadio del colera asiatico*, Firenze.

⁶⁷ Pacini, F. (1880) *Del processo morboso del colera asiatico*, Firenze.

⁶⁸ R. Hermann was chemist to the Institute of Artificial Mineral Waters in Moscow. He was the first to make analyses of the blood of cholera patients, to point to the loss of water from the blood, and to argue from this that bleeding must be a harmful form of therapy.

watery dejections; that if the rate of transudation from the intestine exceeded that of absorption and reabsorption the blood and soft tissues would become progressively depleted of water; and that there were subclinical infections that could result in the spread of infection by apparently healthy human carriers.

On the last point, the following excerpt from a recent publication of the World Health Organization is of interest:

Until about 1960, cholera was considered to occur only as an acute, often highly fatal, infection, with purging diarrhoea. It is now clear that the infection is more often asymptomatic, or produces only a mild diarrhoeal disease...⁶⁹

A synthesis of Snow's epidemiological investigations and reasoning and Pacini's deductions from his microscopical and clinical observations, both made in the year 1854, would have provided a complete answer to the riddle of cholera. It is surprising that William Farr, who was favourably impressed by the findings of both of these pioneers, did not appreciate how conclusive such a synthesis would have been.

The fifth of the International Sanitary Conferences was unique in several respects. It had no logical connexion with either preceding or succeeding conferences; it was the only one to be held in the Western Hemisphere; it was nominally the most internationally representative of all the conferences of the nineteenth century, including participation for the first time not only by the USA but also by 7 Latin American countries, as well as Haiti, Hawaii, China, Japan, and Liberia. But the 26 participating governments, with the exception of "special delegates" sent by 4 governments, were all diplomatic representatives already serving their countries in the USA. The "special delegates", who were all physicians, were sent by Britain (from Canada), the Netherlands, Portugal, and Spain. One of the two such delegates sent by Spain was the illustrious Dr Carlos Finlay, who represented the special interests of Cuba and Porto Rico. The conference opened on 5 January 1881 and lasted for nearly two months, holding only 8 plenary meetings. At the second of these, the Russian delegate proposed that the conference proceedings should be issued in English and French simultaneously, and this was so agreed, this being the only one of the 14 International Sanitary Conferences to have its proceedings issued in any language other than French.

The sole objective of the USA in convening this conference was to obtain international assent to a piece of domestic legislation that would otherwise be unenforceable. On 2 June 1879 Congress had

approved an Act "to prevent the introduction of contagious or infectious diseases into the United States". This act reflected the concern felt at the "extensive prevalence of yellow fever in certain parts of this country during the past two years, and the almost continual existence of the danger of the introduction of such contagious or infectious diseases as yellow fever and cholera by vessels coming to this country from infected ports abroad".⁷⁰ The difficulties in putting the Act into effect arose from its provisions, which required that a vessel whose destination was the USA should be in possession of a certificate in duplicate from a United States consular official "setting forth the sanitary history of the said vessel". Moreover, the consular official was required to satisfy himself as to the truth of the facts stated on the certificate, and the only practical method of so doing was to inspect the ship. The practical implication of this law was therefore that a ship in its home port could not leave for the USA before it had been boarded, inspected, and given a bill of health by the agent of a foreign power. It is hardly surprising that difficulties arose in the enforcement of such a law, and it was evidently the realization on the part of Congress that the Act must necessarily remain a dead letter unless other nations could be persuaded to agree to it that led to the idea of an international conference. In such circumstances it was inevitable that the conference should not be a forum for the discussion of scientific theories but that it should, in the words of the special delegate representing Canada, "assume essentially the character of being administrative". The origin of the conference is to be found in a joint resolution of the Senate and the House of Representatives of the USA, approved on 14 May 1880 and declaring:

That the President of the United States is hereby authorized to call an international sanitary conference to meet at Washington, District of Columbia, to which the several powers having jurisdiction of ports likely to be infected with yellow fever or cholera shall be invited to send delegates, properly authorized, for the purpose of securing an international system of notification as to the actual sanitary conditions of ports and places under the jurisdiction of such powers and of vessels sailing therefrom.

At the second session of the conference on 12 January, a medical delegate of the USA, Dr J. L. Cabell, spoke of the growing conviction of his country's health authorities that too little attention had been paid "to the condition of

⁶⁹ Barua, D. et al (1970) *Cholera control*. In: Araoz, J. de et al., *Principles and practice of cholera control*, Geneva, World Health Organization (Publ. Hlth Pap., No. 40).

⁷⁰ United States of America, Department of State (1880) *Memorandum of July 29, 1880*, Washington (Text annexed to the proceedings of the International Sanitary Conference held in Washington in 1881).



The fifth International Sanitary Conference in Washington in 1881 was the only one ever to be held in the Western Hemisphere. It was convened by the United States in an unsuccessful attempt to persuade other maritime nations that their ships should not sail from their home ports for North America before being inspected and certified as healthy by US consular officials. Almost all of the 26 countries participating in the conference were represented by diplomats already posted to Washington, but 4 of them sent in addition physicians as "special delegates". One of these was the illustrious Carlos Finlay (1833-1915), appointed by the Spanish Government to represent Cuba and Porto Rico, which were then still Spanish possessions. From the very nature of its business, the conference had an essentially political character. Paradoxically, however, this was the only one of the International Sanitary Conferences at which a theory of major scientific importance was for the first time made public, for Finlay declared at it his conviction that yellow fever was conveyed from the sick to the healthy by an intermediate agent. None of the other delegates commented on this challenging declaration, and it was not until almost 20 years later that the final proof of the truth of Finlay's theory was to be provided by the Yellow Fever Commission of the US Army. Finlay's father, Edward, was born in Hull, England, in 1795, studied medicine in France, and later sailed for South America with the intention of joining Bolivar in his struggle for the independence of Venezuela from Spain. However, Edward's intentions were frustrated by a shipwreck, as a result of which he arrived in Trinidad in 1826. There he met and married a girl of French origin, and in 1831 they moved to Cuba. Carlos was a loyal son of Cuba and, like his father before him, a firm believer in independence for the possessions in the Western Hemisphere of colonial European powers. He was, however, conscious of his English descent to the point, according to his son, of insisting on having plum pudding with his Christmas dinner.

vessels, their cargoes, passengers, and crews *at the port of departure*". This lack of precautions in respect of departing vessels, he said, resulted in "a costly application of quarantine restrictions at the port of destination". To remedy this situation, he continued, each government should take steps to obtain

seasonable and accurate information of the sanitary conditions of ports and places in its territory, and promptly to communicate such information to the other parties to the Conference.

Moreover, consuls of foreign governments should be given access to: all hospitals and all the records of the public health, as well as authority to make a thorough examination of vessels, both before and after taking in cargo, when such vessels are about to sail for any of the ports of the country represented by the examining officer.

Developing this plan, Cabell explained that the examination proposed for the point of *departure* "is just that made by the quarantine authorities at the point of destination" and that the "transfer of this inspection" would lessen "obstructions to commerce". This revolutionary, and naïve, pro-

posal that the USA (and other countries) should have the right not only to inspect foreign ships on their arrival in United States (and other) ports but also on departure from their home ports must have caused some consternation among the delegates of the other countries. France asked

if the propositions presented were submitted as an expression of the views of the government of the United States, or were simply put forward as the propositions of the delegates of the United States?

To this Cabell replied that the latter was the case. This was indeed a strange answer, as the American proposal amounted to nothing less than a request to other nations to endorse a law passed by Congress, this law being applicable not only to the USA and its territorial waters but to any country in the world with which the USA had maritime communications. Moreover, in seeking to convene the conference, the Department of State had proposed that delegates should be "authorized to conclude . . . an International Convention", or, in other words, that they should be plenipotenti-

ries, speaking for their governments rather than for themselves. Such a proposal had no hope of success, and was defeated. The only concession to it was a resolution voted by a majority of 11 to 7—with the USA among the dissidents—that bills of health should be delivered at the port of departure by “the responsible sanitary agent of the central government”, but that the

consul of the country of destination shall have the right to be present at the examination of ships . . . under such rules as may be laid down by international agreement or treaty, and the authority to authenticate the bill of health and to add thereon such remarks as he may deem necessary.

Another major proposal was for the establishment in Vienna and Havana of “a permanent international Sanitary Agency of Notification”. The Vienna branch of the agency was to collect epidemiological information from Europe, Asia, and Africa, while that at Havana would be concerned with the Americas. The contracting governments would “have the right to establish, if necessary, a third agency in Asia”. The annual budget of the agency was to be fixed by the governments of Austria-Hungary and Spain, and participating countries were to contribute to it in proportion to their population and their tonnage of merchant ships. Thirteen countries, including Austria-Hungary and Spain, voted for the acceptance of a draft convention providing for the establishing of such an agency. The convention was to be in force for ten years, but any government was to be free to renounce it after three. France, Japan, and the USA voted against such a convention, Mexico and Sweden/Norway abstained, Britain was absent, and the proposed agency never came into being. Resolutions were passed on six other administrative proposals of less importance, always with a divided vote, and although 22 powers signed the final act of the conference on 1 March their signatures represented nothing more than a confirmation that the act was a true record of disagreement. In the special circumstances in which this conference was convened, and with the con-

sequent massive preponderance of diplomats among the participants, it is hardly surprising that its debates did not reflect current thinking on scientific aspects of epidemic diseases. There was, however, one very notable exception. At the seventh session of the conference on 18 February, Carlos Finlay made the first public announcement of his theory that yellow fever was communicated from one person to another by a third intermediate agent:

We have on one side the contagionists, and on the other the non-contagionists, each endeavouring to deny the importance of the cases brought forward by the contrary part in support of their respective opinions. Well, gentlemen, I declare that it is impossible for an impartial mind to look into the stated facts without arriving at this conclusion, that many of the proofs cited in favour of each of those two apparently contradictory opinions must be accepted as perfectly authenticated facts, which conclusion necessarily leads to this other consequence, that we must admit the intervention of a third independent condition in order to account for those two orders of facts.

It is my personal opinion that three conditions are necessary in order that the propagation of yellow fever shall take place:

1. The presence of a previous case of yellow fever within certain limits of time, counting back from the moment that we are considering.
2. The presence of a person apt to contract the disease.
3. The presence of an agent entirely independent for its existence both of the disease and of the sick man, but which is necessary in order that the disease shall be conveyed from the yellow-fever patient to a healthy individual.

While admitting that this was “a mere hypothesis”, Finlay declared his belief that it was a plausible one. It was not until six months later that he was to suggest that a mosquito was the vector of the disease. No discussion of Finlay’s hypothesis followed his statement, but the conference went on to vote by 14 for, none against, and 4 abstentions (Italy, Japan, Russia, Sweden/Norway) that “a temporary scientific sanitary commission will be established by the nations most deeply interested to protect themselves against yellow fever”. This commission never materialized.

The sixth conference: Rome, 1885

With the closing of the Washington meeting, five International Sanitary Conferences had taken place over a span of three decades. France had taken the initiative in convening or initiating the first three, and Russia and the USA the fourth and fifth respectively, in both cases largely for reasons of self-interest. No international treaty emerged from any of these conferences. At the first two, completely contrary views were held about the communicability of cholera, but there was fair degree of agreement on plague and yellow fever. With the third and fourth conferences, although cholera was the only disease under discussion, there was substantial agreement on scientific questions, to the extent that the limited knowledge of the time permitted, and countries that had earlier flatly denied that cholera was contagious—notably Austria, Britain, and France—joined in a unanimous vote that it was transmitted by man. The fifth conference was, apart from the epoch-making declaration of Carlos Finlay, scientifically sterile.

France had not only originated the idea of the International Sanitary Conferences but, some years before the first of them, actively instigated improvements in the sanitary policing of the Levant by providing French physicians to Turkey, initially with a view to preventing invasions of plague and later as a means of arresting also the march of cholera as near as possible to its source. By the time the sixth of the International Sanitary Conferences opened in Rome in 1885, the dawn of the bacteriological age, which would ultimately—but not for many years—put an end to long-standing controversies between contagionists and anti-contagionists, had begun to shed its first light.

In 1882, Koch had demonstrated the existence of the tubercle bacillus and, at about the same time, perfected the use of the solid media that so greatly facilitated the isolation of microorganisms in pure culture. In 1883, there was an outbreak of cholera in Egypt. This prompted Pettenkofer to publish in a general newspaper, the *Münchener Neueste Nachrichten*, an article on "The cholera danger in Munich", which a medical journal "felt obliged" to reproduce *in extenso*.⁷¹ Though the origin of cholera, said Pettenkofer, was still obscure in many

points, research had established several fundamental facts that were beyond doubt.

In its epidemic spread, cholera is not merely dependent on an infectious material (we would say from a cholera fungus that has not yet been discovered) spread by travel, but also on the receptivity of the locality to which the cholera germ is brought.

Moreover, localities might be immune at some times and not at others. There was, therefore, not only a topographical (*örtliche*) but also a temporal (*zeitliche*) disposition to cholera. Cholera infection, he said, originated essentially not from cholera patients but from cholera localities.

Ships transport unripe cholera germ from cholera localities, but the germ must, in order to multiply and become infectious, first be brought again to land, where its development depends on the topographical and temporal disposition.

Thus did Pettenkofer continue to hold as unswervingly to his views as Pacini—who died in 1883—had held to the true explanation of the etiology and pathology of cholera.

In the summer of 1883, both the French and German governments sent medical missions to Egypt to investigate on the spot the cholera epidemic, already past its peak by the time they arrived. The French Chamber of Deputies, and later the Senate, had voted a credit of 50 000 francs for the mission, which arrived in Alexandria on 15 August. The initiative for such a mission had come from Louis Pasteur, and it consisted of four of his disciples—I. Straus, E. Roux, E.-I.E. Nocard, and L. Thuillier. They performed a total of 24 autopsies, and made microscopic examinations of the rice-water stools⁷² and vomitus of cholera patients and of the intestines of the recently dead. In an attempt to produce experimental cholera in animals, they

⁷¹ Pettenkofer, M. von (1883) *Breslauer ärztliche Zeitschrift*, 5, 157.

⁷² The term that they used was *selles riziformes*, which implies that the stools resemble rice rather than rice-water. In 1832, J.-M. Delpuch, who held the Chair of Surgery at Montpellier, visited England and Scotland to study cholera before it had made its first appearance in France. Delpuch, who did not know English (he was accompanied by an interpreter), used "*liquide oriziforme*" as the French equivalent for "rice-water stools" in his book *Etude du cholera-morbus en Angleterre et en Ecosse pendant les mois de janvier et février 1832*, published in Paris in 1832. While the stools in cholera could be (but are not) rice-shaped, it is hardly possible to imagine a rice-shaped liquid. The term *selles riziformes* is still in general use.

introduced by means of a rubber catheter stools and vomitus from cholera patients into the alimentary tracts of guinea pigs, rabbits, mice, chickens, pigeons, quails, a jay, a turkey, several pigs, cats, dogs, and a monkey, but in no case was any cholera-like disease produced. The epidemic of cholera was now waning, and on 14 September Nocard and Thuillier turned their attention to the examination of the bodies of some oxen that had died of cattle plague. On 17 September Thuillier had a loose stool, but before going to bed had a swim and ate a good evening meal. At 3 a.m. on the 18th, he was awakened by the need to pass another loose stool, after which he went into the room of one of his colleagues, crying "I feel very ill", and collapsed on the floor. He recovered and was put to bed, but at 5 a.m. he had another copious watery stool, and by 8 a.m. he appeared to be almost moribund. His colleagues—all of them medical scientists of distinction—intervened by treating him with iced champagne, energetic frictions of the extremities, and subcutaneous injections of ether. These interventions, with the possible exception of the champagne, had as little chance of averting death as the treatments of half a century before,⁷³ but at least they did little to hasten it. A spark of life remained in the patient, until it was extinguished on the morning of the 19th.⁷⁴ Thus, at only 27 years of age, died a brilliant young French medical scientist, Louis Thuillier, to whom Pasteur was to pay homage at a meeting of the Paris Academy of Medicine on 27 November. Roux found this tragedy inexplicable, as none of the French team had been in contact with a case of cholera for 15 days. Moreover, they had all strictly observed the precautions that Pasteur had enjoined upon them before their departure.

On 7 October, the remaining three members of the mission left Egypt, and on 10 November they presented to the Société de Biologie of Paris, in Thuillier's name as well as their own, a brief account⁷⁵ of their findings, publishing them *in extenso* in the following year.⁷⁶ The macroscopic findings that they reported were the same as those of many earlier investigators, with one exception. The mission had been struck by the contrast between the general desiccation of the body on the one hand and the abundance of cerebrospinal fluid on the other, but they did not explain this, as Pacini had done some years before, as the joint effect of atmospheric pressure and the incompressibility of the bony structures in which the fluid was contained. As for microscopic findings, they saw organisms of many kinds, and concluded:

It is evident that, in the presence of such a great variety of organisms, it is impossible to single out and designate the

one that, any more than another, might be the cause of cholera.

They did, however, make special mention of a "slender bacillus" about 0.002 mm in length that was preponderant "at certain points" and invaded the small intestine as far as the submucosa without ever penetrating into the blood vessels or the tunica muscularis of the intestine. This, they add, was doubtless the bacillus described in the reports of Robert Koch, leader of the German mission, which he was evidently inclined to consider as the characteristic organism of cholera. But in some fulminating cases of cholera, this organism could not be found. The final conclusion of the French mission was that:

We do not believe ourselves authorized to attribute a specific action to the microbe that we have encountered in the greatest abundance in the greater number of cases.

However, the members of the French mission thought that they had seen in the blood of cholera patients small bodies that might be microbes and might have some causal relation to the disease, but Koch was probably right in stating that these were blood platelets.

The German mission, including in addition to Koch, Gaffky, Fischer, and a chemist Treskow, arrived in Alexandria on 24 August.⁷⁷ On 17 September—the day that Thuillier was taken ill—Koch sent his first report to the German Minister of the Interior.⁷⁸ The Egyptian authorities had been most cooperative and provided accommodation in the Greek Hospital for bacteriological work and for the housing of animals. Investigations had been made on 12 cholera patients and 10 recently dead from cholera. The blood, lungs, pancreas, kidneys, and liver were free from microbes, and the vomitus contained very few. In contrast, an extraordinary number of microorganisms of the most different types were seen in the stools and intestinal contents, with no one variety preponderating. Conversely, a specific sort of bacterium was found in the wall of the small intestine in cholera victims, but not in those who had died from other causes.

Although it was seen in autopsies on only 10 cholera victims, Koch reported that this finding was so constant that there could

therefore be no doubt that they [the bacteria] stand in some relation to the cholera process. Nevertheless, it is not to be concluded from the association of the latter with the presence

⁷³ For an account of these, see: Howard-Jones, N. (1972) *J. Hist. Med.*, 27, 373.

⁷⁴ *Lancet*, 1883, 2, 697.

⁷⁵ *C. R. Soc. Biol. Paris*, 1883, 35, 565.

⁷⁶ *Arch. Physiol. norm. path.*, 1884, 3rd series, 3, 381.

⁷⁷ *Dtsch. med. Wschr.*, 1883, 9, 485.

⁷⁸ *Dtsch. med. Wschr.*, 1883, 9, 615.

of bacilli in the intestinal mucosa that the bacilli are the cause of cholera. It could be the other way round, and it could equally well be that the cholera process results in such a disruption of the intestinal mucosa that the infiltration into the tissue of the intestinal mucosa of a particular kind of bacillus, among the many parasitic bacteria that exist in the intestine, is made possible. Which of these two points of view is correct, whether the infection process or whether the bacterial invasion is primary, can be determined only by attempts to isolate the bacteria from the diseased tissues, grow them in pure cultures, and reproduce the disease by experimental infections in animals.

To elaborate on Koch's argument: isolation of the organism and its growth in pure culture was not an end in itself. This could be done with any microorganism, whether or not it had any causal relation to cholera. The purpose of growing a pure culture was to demonstrate whether or not it was possible to reproduce the disease in animals by an infection with a particular microorganism and *only that* microorganism. However, Koch did not wait until he had grown pure cultures to initiate attempts at infecting monkeys, dogs, and hens with cholera

material. Recalling the claims of Thiersch in 1856 to have produced experimental cholera in mice, as Koch says incorrectly, "by feeding them with cholera intestine", he had brought 50 mice with him from Berlin in order to try to repeat Thiersch's results. Koch mentions that J. Burdon Sanderson, in England, had thought that he had vindicated Thiersch but Koch himself was unable to do so, all his experiments on mice and other animals remaining "entirely devoid of results". By early October, cholera had died out in the towns and persisted only in some villages of Upper Egypt, but Koch was warned that he would be exposing himself to serious danger from the population if he were to perform autopsies in these villages. In Syria, too, cholera had made little progress, and Koch thereupon resolved that the German mission should proceed to Bombay. But cholera had also died out there, and, sending from Suez his second report on 10 November, he explained why he had requested, by telegraph, approval for going instead, on the advice of several English officials, to Cal-



Robert Koch (1843–1910) was a member of the German delegations both to the sixth (1885) and the eighth (1893) International Sanitary Conferences. In 1884 he confirmed in Calcutta the explanation of the etiology of cholera that Filippo Pacini of Florence had proclaimed for 30 years, naming the pathogen as the *Kommabacillus*. Pacini had died the year before, and Koch nowhere referred to his work, and was perhaps unaware of it. Whatever may be the reason, Pacini's pioneer observations and deductions fell into oblivion, and on Koch's return to Berlin he enjoyed a triumphant welcome as the man who had solved the riddle of cholera. Nevertheless, in other countries, and among some schools of thought in Germany, there was profound scepticism about Koch's contentions. Many leading medical scientists and administrators, especially in Great Britain and British India, rejected his conclusions outright, refusing to accept that the cause of a disease that had such a dramatic impact was simply the oral ingestion of a pathogenic microbe. In the face of such retrograde attitudes, Koch's interventions at the conference of 1885 were minimal, but by the time that he participated in the 1893 conference there was general recognition of the truth of his contentions at the governmental level, if not elsewhere. In 1894, Koch—whose personal experience of International Sanitary Conferences had hardly been encouraging—denounced international discussions of maritime quarantine as "quite superfluous", pointing out that cholera had almost invariably reached Europe from India by land. For Koch, the only solution to the cholera problem was for each State to "seize cholera by the throat and stamp it out". Eighty years later, there are few who would disagree with Koch's contention, and although cholera was the first disease to be subject to International Sanitary Regulations there is room for doubt as to whether this administrative measure has ever prevented a single case of the disease.

cutta.⁷⁹ In the meantime, further attempts at infecting monkeys, dogs, mice, and hens, including injection of cholera material *per rectum*, had proved quite abortive. After nearly two months in Egypt, therefore, Koch had not been able to meet the criteria that he had himself laid down for establishing a microbial cause for cholera.

Chambers claimed in 1938, and Pollitzer endorsed this claim in 1959, that the French and German missions to Egypt had "approached the problem from different angles. Koch, the pupil of Henle, . . . quite naturally approached the problem as a microscopic anatomist who had turned microbist . . . Roux, the pupil of Pasteur . . . set out first to reproduce the disease in animals."⁸⁰ This claim is completely at variance with the facts. The approach of both missions was identical: to find the specific microbial pathogen and to reproduce the disease experimentally in animals. Both missions saw the vibrio and neither had, before leaving Egypt, incriminated it as the cholera pathogen, nor had they succeeded in producing experimental infections in animals. In fact, as will be seen below, seven weeks after he had sailed for Calcutta, Koch reported that it was necessary to determine whether or not the vibrios were normal intestinal flora. Koch's third report was not published, but in his fourth, dated 16 December, he announced that the mission had arrived in Calcutta on 11 December, having left Egypt on 13 November.⁸¹ On the following day the mission met Surgeon-General J. M. Cunningham, whose anti-contagionist views had gained Pettenkofer's approbation but who nevertheless made all necessary facilities readily available.

In his report, Koch outlined a most ambitious programme for the mission. They were to make microscopic examinations of as many cadavers as possible to see whether the bacteriological findings were the same as those in Egypt; to repeat attempts at infecting various animals; to grow pure cultures of microbes and use them for experimental infections of animals; to study the biology of the microbes; to perform disinfection trials; and to investigate soil, water, and air in endemic cholera districts. Moreover, they were also to make a special study of "cholera relationships" by reference to: special characteristics of the population and its environment in endemic cholera areas; outbreaks in prisons, among troops, and on ships; differences between endemic and non-endemic districts; mode of spread of cholera outside endemic districts in and beyond India, and especially the influence of religious customs, pilgrimages, and maritime and land trade routes; and they were to study the measures taken in

India to limit the spread of cholera in prisons and among troops.

In his fifth report, dated 7 January 1884, Koch confirmed that the bacteriological findings in India were the same as those in Egypt, and announced that he had been successful in isolating the characteristic bacilli in pure culture.⁸² It would now be possible, he said, to test

whether these bacilli are normal inhabitants of the intestine, or whether they occur exclusively in the intestines of cholera patients.

Should the latter prove to be a constant finding, it would hardly be possible to doubt the causal relationship of the bacillus to the disease, even should it not be possible to reproduce cholera in animals. This statement constituted a renunciation by Koch of one of his own basic criteria, which he had reiterated only three weeks before in his previous report, for establishing a cause-and-effect relationship between a microbe and a disease. He added the comment that before 1870 the cholera mortality in Calcutta had been 10.1:1000 but that it had since fallen to 3:1000:

It is the unanimous opinion of all the doctors here that the decline of cholera can be ascribed only to the introduction of piped supplies of drinking-water.

In his sixth report—made nearly a month later, on 2 February⁸³—Koch stated that the characteristic bacillus of cholera was not straight like other bacilli, but slightly curved, like a comma. This bacillus he had found without exception in 22 cholera patients and 17 dead of cholera. This, together with the findings in Egypt, justified the conclusion that this bacterial species was constantly present in cholera. Conversely, the bacillus was never found in examinations of the intestines of 28 cadavers who died from other causes, 11 of them from dysentery. This justified the further conclusion that the bacillus was to be found only in cases of cholera.

Koch then posed the question: what is the nature of the relationship of the bacillus to the cholera process? Either that

this specific kind of bacterium merely has its growth favoured by the cholera process and for this reason is so strikingly associated with cholera, or that the bacterium is the cause of cholera and the disease is produced only when the specific bacterium has found its way into the intestines of man.

⁷⁹ *Dtsch. med. Wschr.*, 1883, 9, 743.

⁸⁰ Chambers, J. S. (1938) *The conquest of cholera*, New York.

⁸¹ *Dtsch. med. Wschr.*, 1884, 10, 63.

⁸² *Dtsch. med. Wschr.*, 1884, 10, 111.

⁸³ *Dtsch. med. Wschr.*, 1884, 10, 191.

Pursuing his argument, Koch maintained that the first explanation was not admissible. If it were true, a cholera patient must already have had the bacillus in his alimentary tract. But this could not be the case, as the comma bacillus was found only in cholera cases, and not even in clinically similar diseases such as dysentery and catarrhal diarrhoea. Had these bacilli belonged to the normal intestinal flora they would have been observed before. So, as the growth of these bacteria cannot be due to cholera, only the second supposition remains: that they are the cause of cholera. A number of other facts unmistakably support this view. The bacteria are found essentially in the seat of the disease, the intestine, and hardly ever in the vomitus. They are relatively rare in the first faeculent dejecta, but become so predominant in the rice-water stools that they are almost a pure culture. In patients who recover, the comma-like bacilli gradually disappear.

It would, Koch adds, be desirable to reproduce the disease in animals, in order to have a direct demonstration of a causal relationship, but this had not yet proved to be possible and it must be asked whether it ever will be, as all evidence indicates that animals are not susceptible to cholera infection. Were there a susceptible species, one would expect to find it in Bengal, where cholera exists throughout the year, but no animal infections have ever been seen. The proof afforded by the facts already cited "is not weakened by the failure of the animal experiments". The same was true of other infectious diseases, such as typhoid and leprosy.

Reverting to the characteristics of the bacillus, Koch observes that one of the most remarkable phenomena is its ability to proliferate in soiled linen kept in moist conditions for 24 hours, or in damp earth.

Another very important property of cholera bacteria is that they die so quickly after drying, as does almost no other kind of bacteria. Usually, all life in them is extinguished after drying for three hours.

Another characteristic property was the need for an alkaline medium. Only a very small amount of free acid, harmless to other bacteria, would inhibit their growth. This, and their intolerance to drying, explained why direct contact with cholera patients so seldom resulted in infection.

In his seventh and last report, from Calcutta, dated 4 March, Koch announced that he had isolated the comma bacillus from the tanks where the villagers obtained their drinking-water, and which they also used for their ablutions and for washing clothes—often those of cholera victims.⁸⁴ Further experiments on the bacillus had shown

that it could develop and spread only in moist conditions. Concluding his report, Koch says:

Unfortunately further investigations on this subject must be abandoned because of the premature hot weather this year. In the last weeks, the temperature has been so high that laboratory work could be done only with great difficulty. But it has become intolerably hot in the last few days, and there is no choice but to interrupt the work.

While in India, Koch and his collaborators had carried out investigations on 28 cholera patients and 42 who had died from the disease, bringing their total score since they left Germany to 40 and 52 respectively.

On 2 May 1884, the German mission arrived in Berlin, having, at the behest of Koch, broken their journey in Munich in order to visit "Chairman of the former Imperial Cholera Commission Royal Bavarian Privy Councillor Higher Medical Councillor Herr Professor Dr von Pettenkofer" to acquaint him personally with the results of the expedition. Neither Koch nor Pettenkofer has left any record of what passed between them.

On 26 July 1884 a "Conference for the Discussion of the Cholera Question" opened in Berlin, attended by a galaxy of German medical scientists, including von Bergmann, Eulenberg, Gaffky, Hirsch, Koch, and Virchow, Pettenkofer being conspicuous by his absence.⁸⁵ Koch, the principal speaker, began by referring to the contradictory opinions that still reigned as to the nature of cholera, its method of spread, the possible role of the soil and, in particular, the significance of drinking-water as a vehicle for the infectious material. The discussion lasted for several hours, most of this time being devoted to an extremely detailed exposé by Koch of the findings and conclusions of the German Cholera Commission. Koch's contention that the cholera vibrio was the specific causative agent of the disease met with no opposition, although Virchow sounded a note of caution in pointing out that absolute proof was as yet lacking. With regard to the pathology of the disease, as Gaffky reported three years later, the German mission concluded that the toxin of the cholera vibrio had a dual action, in that it directly affected the intestinal epithelium while at the same time being absorbed into the bloodstream and exerting a paralysing effect on the circulatory system. "The symptom complex of true cholera attacks," said Gaffky, "which is usually regarded as a consequence of loss of water and thickening of the blood, is in my opinion to be considered

⁸⁴ *Dtsch. med. Wschr.*, 1884, 10, 221.

⁸⁵ *Dtsch. med. Wschr.*, 1884, 10, 499, 519.

essentially as an intoxication.”⁸⁶ Here was a long step backwards, for when cholera had first invaded Europe over half a century before, many physicians were so struck by the appearances of the heart and blood vessels in dehydrated cadavers that they were misled into believing the disease to be primarily a cardiovascular affection. In fact, F. C. M. Markus, secretary to the Temporary Medical Council that had been appointed in 1830 to advise on cholera in Moscow under the Chairmanship of its Governor-General, Prince Dimitri Vladimirovich Galitzin, proposed that a more suitable name for the disease would be *Cardiognmus vitalis epidemicus*.⁸⁷

Reviewing the discussions at the Berlin cholera conference, the editor of a leading German medical journal, Dr P. Börner, expressed the hope that Pettenkofer's thinking would take a new direction in consonance with the new facts that had come to light.⁸⁸

One who has worked successfully in so many fields of hygiene as he, always stimulating, instructive, and creative, has all the less reason to fear to make a concession in respect of one field.

Börner's sage counsel fell on deaf ears, however, and Pettenkofer preferred to proclaim to the last the need for some sort of maturation of the cholera vibrio in an appropriate soil before it could become harmful to man. Writing to the general press a month after the Berlin conference, he reiterated:

I maintain, supported by a large series of facts collected and confirmed both in India and here, the dependence of cholera epidemics on place and time. There are places, and there are times, where cholera, although disseminating among many individual cases, does not flourish . . . Koch's discovery of the comma bacillus alters nothing, and, as is well known, was not unexpected by me.⁸⁹

Whatever may have been the scepticism of Pettenkofer and his followers, elsewhere in Germany Koch was treated as a national hero. A banquet with 700 guests was held in Berlin for members of the commission, and the Kaiser awarded the Order of the Throne (Second Class), with Star, to Koch, and the Order of the Red Eagle (Third Class) to Gaffky and Fischer, all these decorations being personally bestowed by the Crown Prince. The Imperial Health Office presented Koch with a lifesize bust of the Kaiser, and Gaffky and Fischer with “magnificent photographs” of their Sovereign.⁹⁰ Moreover, Parliament voted a monetary award to the commission of 135 000 marks.

In other countries, the reaction could hardly have been less enthusiastic. The French medical press reflected the views of the French mission to Egypt. One medical journal even declared: “The great microbe hunter has followed a completely false

trail. (Will he give back his decoration?)”⁹¹ Showing much more moderation, a French physician reported to the Paris Academy of Science that he had made five large pills out of 5 cm³ of fresh rice-water stools mixed with lycopodium and gum, and swallowed them all.⁹² After this, he had fever for 24 hours and constipation. This experiment showed, he said, that:

The gastric ingestion of the diarrhoea fluid of cholera containing comma bacilli does not necessarily produce cholera.

Such a conclusion was hardly worth making, far less reporting, for it must have been perfectly obvious to everybody that in the worst epidemic of any communicable disease, only a small minority of the population at risk is affected.

A remarkable omission from all Koch's writings on cholera is that he nowhere mentions the pioneer observations of Pacini, who had without any doubt identified the cholera vibrio and incriminated it as the causative organism of the disease, and who had persistently maintained his contentions for almost three decades, until he died in the very year in which the German mission set forth for Egypt. This omission did not pass unnoticed in Italy. On 13 September 1884 Vittore Trevisan published an article “On the bacillus of cholera”, beginning as follows:

Koch . . . has dressed himself in borrowed plumes: when he, “no more, no less”, affirms that he has discovered the bacillus of cholera, discovered thirty years before by Pacini.

And Trevisan then quotes a Milan daily paper as posing the question: “Must we always, we Italians, praise the good that comes from abroad, while for some time we have had it at home?”⁹³ It is incontestable, says Trevisan, that Koch, primarily a bacteriologist, has the merit of having completed the story by isolating the bacillus in pure culture, but it is equally incontestable that Pacini, primarily a pathologist, has the merit of having been the first to give a recognizable description of the organism, to have given evidence of the importance of its action on the intestine, and to have incriminated it as the cause of the disease. There can, he concluded, be no doubt as to the absolute identity of

⁸⁶ Gaffky, G. (1887) *Bericht über die Thätigkeit der zur Erforschung der Cholera in Jahre 1883 nach Ägypten und Indien ersandten Kommission*, Berlin.

⁸⁷ Markus, F. C. M. (1832) *Rapport sur le choléra-morbus de Moscou*, Moscou.

⁸⁸ *Dtsch. med. Wschr.*, 1884, 10, 533.

⁸⁹ *Dtsch. med. Wschr.*, 1884, 10, 575.

⁹⁰ *Dtsch. med. Wschr.*, 1884, 10, 11.

⁹¹ *Le Praticien*, 1884, 6, 497.

⁹² *C. R. Acad. Sci (Paris)*, 1884, 99, 845.

⁹³ *Gazz. med. ital. lombardia*, 1884, 44, 373.

the *Vibrio cholerae*⁹⁴ of Pacini (1854) and the *Bacillus virgula*⁹⁵ of Koch (1884). But this defence of Pacini's right to posthumous recognition appears to have made little impact even in Italy, for in the following month the same journal published an article on cholera in which the author refers only to the comma bacillus of Koch.

In England the *Lancet* raised its voice in defence of Pacini in an editorial of 2 August 1884, quoting first in the original Italian and then in English translation from his 1865 publication:

When my scientific labours, having made the tour of Europe, will have returned, arrayed in foreign garb, to Florence, they will have permission to enter the schools, and then we shall be enjoying the tranquil repose of Trespiano—in our grave in short. This bitter forecast [comments the *Lancet*] has been verified almost to the letter, Pacini's doctrine, rehabilitated by the German Cholera Commission, being now adopted by his compatriots and taught in the Istituto Patologici [96] of Italy a year after his death.⁹⁷

In the USA there was scepticism, and on 12 July the writer of a medical editorial referred to Koch's "microbes", reiterating the long-held opinion that fear disposed to cholera:

The popular germ theories and associate doctrines of contagiousness, greatly exaggerated by the newspaper press, are adding to the terror of all classes of people, and will correspondingly increase the destructive effects of the epidemic wherever it makes its appearance. For of all the predisposing causes of cholera, fear, dread, and mental trepidation are among the most efficient.⁹⁸

The country that had the greatest stake in unravelling the enigma of cholera was Great Britain. Not only was the disease a serious threat to the health of British troops in India, but the British Empire was in the unenviable position of being the purveyor of cholera to the rest of the world. Moreover, it was hardly to the credit of Britain if a German medical mission had indeed, after a stay in India of only a few weeks, elucidated a health problem that was essentially a British responsibility. When Koch's claims became known in Britain, influential voices were raised against them. The *Lancet* reported that Surgeon-General Sir William Hunter, who had served in Egypt during the 1883 cholera epidemic, read a paper before the Epidemiological Society of London in which he declared "his unqualified opinion that the disease was non-contagious, non-specific, and endemic in Egypt".⁹⁹ Hunter believed that the disease resulted from meteorological conditions. Reporting the following meeting of the same society, the *Lancet* says that a Dr Thrupp "did not believe in the 'germ' of cholera, and thought it as great a myth as the sea serpent".¹⁰⁰ Most of the other speakers at the meet-

ing deprecated the idea of contagion. The day before, Sir Joseph Fayrer, Physician to the Council of India, had said that he

entirely disbelieved in the communicability of cholera... no fact ever brought before his notice had suggested the shadow of an idea that cholera was communicated from person to person.¹⁰¹

Most other speakers were of a like view.

Addressing the Annual Meeting of the British Medical Association of July–August 1884, Charles Cameron thoroughly reviewed the findings of both the French and the German missions, and warned in respect of the latter:

We must absolutely refuse, in the interests of public health, to accept them as established premises on which, unsupported, to found practical conclusions.

In Victorian England it was an article of faith that the only safeguard against epidemic diseases lay in an abundant supply of "fresh air", pure drinking-water, sanitary disposal of organic wastes, avoidance of overcrowding, and cleanly and temperate personal habits. The opposition to the idea of a specific contagion was expressed with such conviction that it is hardly possible to doubt its sincerity. Nevertheless, this attitude represented a retrograde step from the unanimous conclusions of the third International Sanitary Conference almost 20 years earlier.

Such was the majority British reaction to Koch's claims. Among the few dissentient voices was that of Surgeon-General W. R. Cornish, Honorary Surgeon to the Viceroy of India. Addressing the South Indian branch of the British Medical Association on 16 February, he welcomed the efforts of the German mission, while deploring that the British Government had failed to take a similar initiative. A few weeks later, an army surgeon, Andrew Duncan, wrote on 26 March from Rawalpindi to the *Lancet* to protest that Surgeon-General Cuninghame, the Sanitary Commissioner for India, was stifling any attempts at research based on the idea of "conveyance of cholera by human intercourse":

we have at the present moment the highly gratifying spectacle, to us as Englishmen, of the etiology of cholera elucidated by our distinguished German visitors, after a few weeks' work on the very spot on which a highly salaried officer,

⁹⁴ *Vibrio cholera* was in fact the name used by Pacini.

⁹⁵ Koch himself had not used this Latinized version of *Kommabacillus*.

⁹⁶ This should have read "Istituto Patologici".

⁹⁷ *Lancet*, 1884, 2, 203.

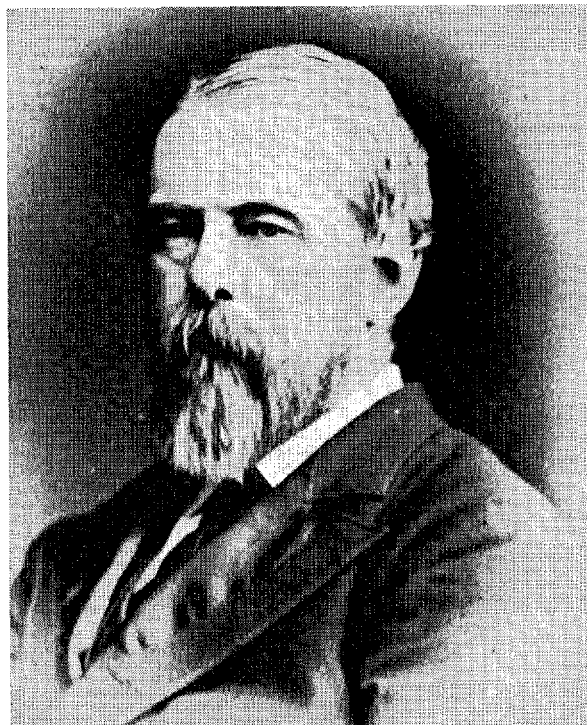
⁹⁸ *J. Amer. med. Ass.*, 1884, 3, 46.

⁹⁹ *Lancet*, 1884, 1, 86.

¹⁰⁰ *Lancet*, 1884, 1, 344.

¹⁰¹ *Brit. med. J.*, 1884, 1, 359.

Sir Joseph Fayrer (1824–1907) was the chief delegate for British India at the sixth International Sanitary Conference. He had studied medicine in London as a fellow-pupil of Thomas Henry Huxley, and after completing his studies he proceeded to Italy where he obtained the M.D., Rome, and then went to Scotland to acquire an M.D., Edinburgh. In addition he received honorary degrees both from Edinburgh and Padua, was a Fellow of the Royal Society and of the Royal Colleges of Physicians and of Surgeons, respectively foreign correspondent and member of the Academies of Medicine of Paris and Rome, and a Fellow of the Philadelphia Academy of Sciences. After a long career in the Indian Medical Service he became President of the Medical Board of the India Office in London. In spite of Fayrer's impressive list of distinctions, his ideas of the etiology of epidemic diseases were on a par with the convictions of the dwindling minority who still believed that the earth was flat. For Fayrer, cholera was but a variant of malaria, both conditions being caused by fluctuations in the electrical tension and degree of moisture of the atmosphere. Four years after Koch's incrimination of the cholera vibrio, and 3 years after the sixth International Sanitary Conference, Fayrer stated: "I demur to a microbe being accepted as the solution of such a problem as the cause of cholera". At the conference itself, he repeatedly "demurred", refusing even to accept that there should be any discussion of "the theory of the transmissibility of cholera". In this atavistic approach, Fayrer received energetic support from the chief delegate for Great Britain, Surgeon-General Sir William Hunter, whose "unqualified opinion" was that cholera was non-communicable, non-specific, and endemic in Egypt. For both these staunch evangelists of obscurantist and anachronistic epidemiological theories, the claims of Robert Koch—who was also a delegate at the conference—were sheer heresy, and they effectively blocked any proposal that would lead to "a theoretical discussion on the etiology of cholera". Reporting after the conference to the Local Government Board, Hunter's fellow medical delegate, Richard Thorne Thorne,



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reassuringly stated that it had been agreed that "all questions involving scientific and theoretical considerations, and especially such as related to the etiology of the disease, should be excluded from the discussion".

especially appointed by the government for sanitary purposes, has for years contented himself with enunciating doctrines totally opposed to all medical logic.¹⁰²

But Cuninghame was not the man to be influenced by such criticisms. Towards the end of 1884, he published a work on cholera in which he asserted: "The water theory is negated not only by the experience of individual places . . . but by the general history of cholera in India year after year."¹⁰³ Moreover, the answer to the question whether ships could convey cholera from India to other countries "must be decidedly in the negative". He gives a very full account of the findings of the German Cholera Commission, but says that "the whole superstructure" that it has raised "has in fact tumbled to the ground", because Koch's bacillus has been found in the saliva of healthy persons and "in other cases besides those of cholera".

In the following year a German edition of Cuninghame's book was published, with a foreword by Pettenkofer, who lauds the author because "he lets only epidemiological facts speak". Cuninghame's

book, says Pettenkofer, is "a cornerstone of epidemiological research".¹⁰⁴

As an editorial writer in the *British Medical Journal* put it: "Till an animal is found that takes cholera, opinions on this matter will be hopelessly divided."

That the British Government was not entirely oblivious to its moral responsibilities is indicated by the fact that it appointed a mission, consisting of two readers in histology, Emanuel Klein and Heneage Gibbes, and a laboratory technician to proceed to India to investigate Koch's claims; they left England on 6 August 1884.¹⁰⁵ In the introductory remarks to their report, published in the following year, on the results of their investigations, Klein and Gibbes refer to Pettenkofer as being "justly considered to be the greatest living authority on

¹⁰² *Lancet*, 1884, 1, 175.

¹⁰³ Cuninghame, J. M. (1884) *Cholera: what can the state do to prevent it?* Calcutta.

¹⁰⁴ Cuninghame, J. M. (1885) *Die cholera: was kann der Staat thun sie zu verhüten?* Brunswick.

¹⁰⁵ *Brit. med. J.*, 1884, 2, 292.

cholera", and the report as a whole constitutes a flat refutation of Koch's contentions.¹⁰⁶ In support of their negative conclusions they cite the small number of comma bacilli found in some cases of cholera and the presence of other microorganisms in large numbers. Moreover, organisms similar to the comma bacilli had been found in cases of diarrhoea in Europe, as also in the healthy mouth.¹⁰⁷ As for the role of drinking-water as a vehicle, they maintained:

There exist on record a good many cases in which water, as the vehicle of the virus, is put forward as having been proved, but the majority of these, on critical examination, do not stand.

The British Government, in the person of the Secretary of State for India, appointed a committee to consider the Klein-Gibbes report. In the "transactions" of this committee, which included such eminent members as Professor John Burdon-Sanderson, Sir Joseph Fayrer, Sir William Gull, Sir William Hunter, and Sir William Jenner, Gull is credited with saying that he

considered that it had long been demonstrated that cholera as cholera does not produce cholera ... The presence of cholera depended on conditions of locality ... It appears to be abundantly proved that cholera is not an infectious or contagious disease.

Several other speakers supported Gull, and 8 of the 13 committee members appended written memoranda endorsing the refutation by Klein and Gibbes of Koch's contentions.

A second conference "for discussion of the cholera question", under the chairmanship of Virchow, opened in Berlin on 4 May 1885.¹⁰⁸ This time Pettenkofer was present, in addition to Bergmann, Eulenberg, Gaffky, Hirsch, and Koch, to name only the most prominent participants. Koch opened the discussion by challenging the claims of Finkler and Prior, Klein, and Emmerich to have identified the comma bacillus elsewhere than in cases of cholera. He also reported experimental cholera infections in guinea pigs. In these experiments the gastric juice of the animals had first been neutralized with 5 cm³ of a 5% solution of sodium bicarbonate, and after an interval of 20 minutes 10 cm³ of a broth-culture of cholera vibrios were introduced into the stomach. Immediately afterwards a tincture of opium (strength not stated) was injected intraperitoneally in a dose of 1 cm³ per 200 g of body weight. The animals became unconscious for 30-60 minutes and then recovered, and on the following day they fell ill, dying after 1-3 days. Post-mortem examination showed the alimentary tract to be full of a colourless

fluid that was "almost a pure culture of comma bacilli". Therapeutic experiments showed, according to Koch, that large doses of calomel, or naphthaline, prolonged life in most cases by one day. Koch was followed by Pettenkofer, who was sceptical of the validity of these alleged experimental infections. And, indeed, although Pettenkofer did not say so, the experiments were very far removed from the circumstances of natural infections in man. If the weight of a guinea pig be taken as rather less than 1 kg, 5 cm³ of sodium bicarbonate solution would be equivalent to almost a pint in a man of 70 kg, and the dose of broth-culture would be almost a quart. And to this would have to be added an intraperitoneal injection of almost a pint of tincture of opium. Koch admitted that the combination of orally ingested alkali and intraperitoneal tincture of opium also increased the susceptibility of animals to other microorganisms. In the circumstances, Koch's experimental infection of guinea pigs with cholera seemed to many to be far from conclusive. The discussions continued for the next four days, and Virchow pointed out that in Koch's experiments the opium might inhibit diarrhoea and vomiting, and that in this respect they did not in a sense reproduce the disease.¹⁰⁹ Further experiments were necessary. Pettenkofer repeated his now familiar view that cholera could not be spread by human intercourse unless in the presence of the appropriate disposition of locality and time.

In standard textbooks of medical history, it is variously stated that Koch "discovered" the cholera vibrio in 1883 or 1884, and the impression is given that this was a breakthrough that was universally recognized as such. Nothing could be further from the truth. Outside Germany there was at first an almost universal refusal to accept Koch's conclusions, and even within Germany Pettenkofer headed an influential faction of epidemiologists, sometimes referred to as "localists", to whom Koch's contagionist explanation of cholera was anathema.

It was in such an atmosphere of open disagreement that the sixth International Sanitary Conference was opened in Rome on 20 May 1885 by the Italian Minister for Foreign Affairs, who explained that Italy had been prompted to convene the conference as a result of the reappearance of cholera in Egypt in 1883.

¹⁰⁶ Great Britain, India Office (1885) *India cholera inquiry by Doctors Klein and Gibbes, and transactions of a committee convened by the Secretary of State for India in Council*, London.

¹⁰⁷ It is true that organisms morphologically difficult to distinguish from *Vibrio cholerae* are quite widely distributed, but their cultural characteristics are different.

¹⁰⁸ *Dtsch. med. Wschr.*, 1885, 11, 329.

¹⁰⁹ *Dtsch. med. Wschr.*, 1885, 11, 242.

A German¹¹⁰ and a British medical journal were equally sceptical about the results of the conference, the former stating: "We do not promise ourselves the slightest result from such a conference" and the latter commenting:

Unfortunately, the decisions of the Conference, if we may judge by the utter want of result from the resolutions of the Vienna conference, will really settle nothing. At the first panic about cholera, the votes of delegates, the resolutions of conferences, and the convictions of sanitary administrators, will again be instantly set aside and repudiated, in response to unreasoning popular clamour.¹¹¹

These words were to find an echo in the contraventions of the International Sanitary Regulations that took place over 80 years later as a result of the seventh pandemic of cholera (regarded by some authorities as the eighth).

By the time the conference opened, over a year had elapsed since Koch's triumphal return to Berlin. Moreover, he attended as one of the three German delegates to the Rome conference. It might therefore have been supposed that this conference would witness an international confrontation of contradictory scientific theories on cholera, and provide a unique opportunity for Koch to develop his ideas before an influential international audience. If any had entertained such a supposition, they could hardly have been more mistaken: in just under 400 folio printed pages of the proceedings there is not a single reference to Koch's comma bacillus, or any discussion of the etiology of the disease. The keynote was struck by the Italian Foreign Minister, when he declared in his inaugural address his belief that the conference would eliminate as far as possible "purely theoretical discussions" in order to give its work an "eminently practical character". In the draft rules of procedure submitted to the conference by the Italian Government, it was provided that "experts" in delegations should be "admitted to sessions by authorization of the Chairman in each special case; they will not have, however, in any case, the right to vote, nor that to speak". The conference accepted the rules as a whole, but this particular one was honoured more in the breach than in the observance.

Twenty-eight countries participated in the conference, Britain and India having separate delegations, both composed of arch-anticontagonists; the former included Sir William Hunter and Dr Richard Thorne Thorne, the medical officer of the Local Government Board, and the latter Sir Joseph Fayrer and a Dr Timothy Lewis.¹¹² In a circular letter of 21 April, the Italian Foreign Minister had indicated that the conference would have a dual

task: "*technico-scientific*" and "*diplomatico-administrative*", and one of the first actions of the conference was to establish a technical committee, which held its first meeting on 23 May. However, the crucial question that a technical committee might have been supposed to put first on its agenda—that of the nature and mode of transmission of cholera—was by common consent decided to be too controversial for discussion, the delegates from Britain and India, in particular, showing a fastidious sensitivity to any reference to the etiology of the disease.

At the committee's second meeting, Sir J. Fayrer "did not wish to make any pronouncement on the theory of the transmissibility of cholera" and his fellow-delegate, Dr T. Lewis, also disclaimed any intention of expressing an opinion on "the origin of the disease and the theory of its transmissibility". At the next meeting, Fayrer denied that cholera had ever been imported into Europe from India, and Hunter challenged anyone who claimed that cholera had been conveyed to the Mediterranean basin by ships coming from that country to "cite the names of these ships, specify their points of departure, and prove that they had indeed introduced cholera into Europe". The challenge was not taken up.

At a later meeting of the committee, Hunter explained that he could not support a proposal of the Italian delegation, because "it would lead to a theoretical discussion on the etiology of cholera and would give rise to numerous divergences of opinion". And at the twelfth meeting of the committee, after a statement by Koch that the incubation period of cholera had been scientifically shown to vary from one to five days, Fayrer threatened that he would withdraw a vote that he had previously cast "if questions of the etiology of cholera and the theory of incubation were admitted to the discussion".

The Italian Foreign Minister had referred in his circular proposing the conference to "the most complete anarchy" that continued to exist in the various quarantine requirements of different countries, and the objective that the conference set itself was to endeavour to reach agreement on the minimum requirements that could safely be accepted, on the strict understanding that there should be no attempt to agree on the nature of cholera or its mode of transmission.

¹¹⁰ *Dtsch. med. Wschr.*, 1885, 11, 264.

¹¹¹ *Brit. med. J.*, 1885, 1, 1014.

¹¹² Delegations from the following countries, in addition to those from Germany, Great Britain, and India, participated: Argentina, Austria-Hungary, Belgium, Brazil, Chile, China, Denmark, France, Greece, Guatemala, Italy, Japan, Mexico, Netherlands, Peru, Portugal, Rumania, Russia, Serbia, Spain, Sweden/Norway, Switzerland, Turkey, Uruguay, United States of America.

The sole disease discussed at the conference was cholera, although the one United States delegate, Dr G. M. Sternberg, succeeded in having a mention of yellow fever added to several resolutions. The main preoccupation with cholera was in connexion with the sanitary regulation of shipping passing from the Red Sea to traverse the Suez Canal. Four-fifths of all the ships passing through the canal were British, and in the year 1884 770 of them had arrived directly at British ports from India and 123 from China, and a considerable number arrived from the East after touching at intermediate ports. Although there were differences of opinion on details, and the same countries did not vote together on all questions, the fundamental issue was whether British maritime traffic coming from cholera-infected areas, chiefly Bombay, and traversing the Suez Canal, should be subject to sanitary control at Suez and, if so, what should be the severity of the control measures. A specific criticism made of the British in this connexion was that, although cholera was always present in Bombay, ships sailing from there were given a clean bill of health unless an "epidemic" had been declared. It was asked: how many cases constitute an "epidemic"? But to this, no answer was forthcoming. Britain and India repeatedly insisted that no control measures were necessary, and on this question they were in a minority of two. Hunter proposed a motion that:

English merchant ships, mailships, and troopships that do not have any communication with Egypt, nor with any [continental] European port should always be able to traverse the Suez Canal, as an arm of the sea, without inspection.

Only Britain and India voted for this motion, Japan and Russia abstaining and 18 other countries voting against it. The technical committee had appointed several subcommittees to consider specific questions, and one of these was on the sanitary control of westward-bound ships from the Red Sea. This subcommittee had recommended that:

If a ship is infected, that is to say, if there are on board one or more cholera patients, the passengers will be disembarked, isolated, and separated into as small as possible groups.

Britain and India voted against this proposal, Japan and Brazil abstained, and 18 other countries voted in favour. Explaining the British vote, Thorne Thorne maintained that no useful purpose could possibly be served by disembarking several hundred passengers in the "dirty and ill-kept lazarets of Egypt", to which the Turkish delegate replied that Indian ports were dirtier than Red Sea ports. England, Thorne Thorne had said,

does not demand specially favourable treatment; but it wishes that each country should act as it sees fit in regard to its own ships.

The question might well have been asked: if every country were left free to make its own arrangements, what was the purpose of the international conference? To such a question, the British could have replied that it was only reluctantly that they had agreed to participate. Great Britain and India both had votes because the conference had decided, as had the Vienna conference in 1874, that votes should be by autonomous health administrations rather than by sovereign powers. Thus, Austria and Hungary were also entitled to separate votes. It would appear from such a decision that Egypt, although forming part of the Turkish delegation, would also have been entitled to a vote, but the Egyptian representative, Dr Abbate Pasha, did not put in an appearance until the fifteenth and last meeting of the technical committee on 7 June, only 6 days before the fourth and final plenary session of the conference. By this time, all voting had been concluded. Even had he appeared earlier, his situation would have been anomalous, for Egypt had been for nearly three years under British military occupation. Moreover, as Adrien Proust, one of the members of the French delegation to the conference, was to complain a few years later, the *Conseil sanitaire maritime et quarantenaire* of Alexandria, upon which several European powers were represented, was dominated by the British.¹¹³

As a sovereign power, Britain was in a minority of one in regard to the crucial questions discussed by the conference; yet, paradoxically, the measures of sanitary control advocated and practised by the British were completely in line with the thinking and practice of today, as exemplified by the International Health Regulations. They repudiated the idea of wholesale incarceration of the passengers and crew of an infected ship. In accordance with the Cholera Regulations published in the *London Gazette* of 13 July 1883, ships from cholera-infected areas arriving at British ports were medically inspected on arrival. Any cholera cases were admitted to hospital and any passengers with suspicious symptoms could be detained for up to 48 hours. All other passengers were free to disembark on giving their names and exact destinations, after which they would be kept under surveillance by the local health authorities. Strict attention was paid to the sanitary disposal or

¹¹³ Proust, A. (1892) *La défense de l'Europe contre le choléra*, Paris, It is difficult to understand Proust's statement that "the Alexandria Council has nothing international but its name" and his reference to "the so-called international Council". The Council's name, as given above, is exactly that given in the Khedival decree of 3 January 1881 that created it. The full text of this decree is reproduced by Gaffky (reference 23).

disinfection of the excreta, clothing, bed linen, and other effects of cholera patients, and it was emphasized that the surest protection against the disease was a sanitary environment, especially a pure supply of piped water and adequate facilities for sewage disposal.

At the fourth and last plenary session of the conference, the President read a communication from the Italian Foreign Minister, Mancini, in which he assented to the desire of a majority of delegates for an adjournment and proposed that the conference should reconvene on the following 16 November. Although the participants unanimously agreed to this date, the conference was never resumed, and it was not until 7 years later that a further conference with much more limited participation was held.

Uncompromising as may seem the British stand at this abortive conference, it was a fact that cholera had never been imported directly into Europe by a vessel reaching the Mediterranean from east of Suez. Moreover, in spite of its close maritime communications with India and the Far East, there had not been an epidemic outbreak of cholera in the British Isles since 1865.

After the adjournment of the conference, the British ambassador in Rome made it quite clear, in a letter¹¹⁴ to its President, that the views of the majority would not prevail as far as British shipping was concerned. The English Government could not understand, he said,

in what way the immediate free passage through the canal that it asked for vessels directly bound for English ports

could be harmful to other countries, provided that the necessary measures were taken to prevent any communication between these vessels and the land.

On the purely practical side, he continued, how would it be possible to handle the arrival of a ship with 1000 or 1500 on board among whom there were one or two cases of cholera? How would they all be divided into small groups and suitably lodged, as recommended by the conference, and what if three or four ships of similar size arrived simultaneously? Then there was the question of the loss of 5 days while passengers and crew were in quarantine. This would reduce to only 2 days the saving of time effected by using the canal instead of rounding the Cape. Already, the canal dues were little less than the additional cost of rounding the Cape. With a 5-day loss of time at Suez, use of the canal would become uneconomic.

This Parthian shot was the epilogue to another fruitless International Sanitary Conference, the last of six, in which differences of opinion were if anything more marked than they had been at Constantinople almost two decades before. Robert Koch had been effectively muzzled but, even had he been able to convince all participants of the etiological significance of his comma bacillus, it is difficult to think that this would have influenced the outcome, for no one at the conference would have questioned that direct or indirect contact with the dejecta of cholera patients was an important factor in the transmission of the disease.

¹¹⁴ This letter is reproduced as an appendix to the published proceedings of the conference.

The seventh conference: Venice, 1892

Shortly after the Rome Conference, the editor of a German medical journal ironically pointed to the "surprising concordance between England's commercial interests and its scientific convictions". The English Cholera Commission, he said, had also found the comma bacillus, "but obstinately denies its significance".¹¹⁵ But there was not unanimous opposition in England to Koch's views. A few days after the conference had adjourned, W. Watson Cheyne, a pupil of Lister, published the last of a series of five instalments of a "Report on the Cholera Bacillus" to the Scientific Grants Committee of the British Medical Association.¹¹⁶ Watson Cheyne had visited Paris to examine cholera material, and in his most exhaustive report he unreservedly vindicated Koch's findings and conclusions, pointing out that Klein had erred in failing to realize that Koch, in his identification of the specific bacillus of cholera, had relied not only on morphological but also on cultural characteristics. Almost simultaneously, J. Burdon-Sanderson,¹¹⁷ then Waynefleete Professor of Physiology and subsequently Regius Professor of Medicine at Oxford, delivered a lecture at the Royal Institution, London, in which he stated that Klein "had sufficiently disproved the theory of Dr. Koch . . . a view which was not supported by any adequate evidence". The promulgation of Koch's doctrine was, he said, an "unfortunate fiasco".¹¹⁸

During the seven years before the next International Sanitary Conference, controversy about the significance of the comma bacillus continued. In France, Maurin and Lange claimed in 1885 that Koch's bacillus was an "epiphenomenon" of the cholera process and that the true cause of the disease was a fungus, to which they gave the name *Mucor cholérifère*, but E. C. Wendt of the USA, writing that this was "heralded in France as a great discovery", dismissed it as a claim upon which comment was "hardly called for".¹¹⁹ W. Nicati and M. Rietsch of Marseilles, on the other hand, confirmed Koch's results in considerable detail.¹²⁰ Also in 1885, the Association for the Advancement of Medicine by Research, the Royal Society of London, and the University of Cambridge jointly sponsored a medical mission to investigate the cholera

epidemic in Spain. The members of the mission were C. S. Roy, J. G. Brown, and C. S. Sherrington—the last of these a young man of 27 who, 47 years later, as Sir Charles Sherrington, shared the Nobel Prize in medicine and physiology with E. D. Adrian. Sherrington also went in the following year by himself to study cholera in Italy. In its report on microscopic observations made and autopsies performed in Madrid, the mission stated that it had found only small numbers of comma bacilli in the intestinal contents and that in many cases they appeared to be completely absent.¹²¹ The bacilli were only rarely to be found in the intestinal mucous membranes. The mission concluded that while the comma bacillus probably had some relation to cholera, these findings, and those of Straus in Egypt and France, and of Klein in India, proved that "it is [not]¹²² the direct cause of cholera". Another finding was that, in some of the patients who had been treated by intravenous infusions, blood examinations at autopsy showed clear evidence of gross septicemia. But it was not only the various treatments used that were adding to the natural hazards of the Spanish epidemic. J. Ferran, of Seville, who believed in Koch's bacillus, claimed that the subcutaneous injection of live or killed cultures of it produced immunity against cholera or, at least, "an extraordinary diminution of the probability of death"¹²³ in those who contracted the disease. Noting these claims in an editorial, the *British Medical Journal* expressed the utmost scepticism. Nevertheless, reports of a Spanish anticholera vaccine aroused much interest in England. The correspondent in Spain of the *British Medical Journal* gave an eye-witness account of the appalling condition of

¹¹⁵ *Dtsch. med. Wschr.*, 1885, 11, 347.

¹¹⁶ *Brit. med. J.*, 1885, 1, 821, 877, 931, 975, 1027.

¹¹⁷ In earlier publications his name was not hyphenated.

¹¹⁸ *Brit. med. J.*, 1885, 1, 1076.

¹¹⁹ Wendt, E. C. (1885) *A treatise on the Asiatic cholera*, New York.

¹²⁰ Nicati, W. & Rietsch, M. (1886) *Recherches sur le choléra*, Paris.

¹²¹ Roy, C. S., Brown, J. G. & Sherrington, C. S. (1887) *Report on the pathology and etiology of Asiatic cholera as observed in Spain in the summer of 1885*, London.

¹²² The "not" is missing in the original, but from the context this is evidently an accidental omission.

¹²³ Ferran, J. & Pauli, J. (1886) *El cólera morbo-asiático: Breves consideraciones sobre la etiología y profilaxis de esta enfermedad*, Sevilla.

Sir John Burdon-Sanderson (1828–1905) was Professor of Physiology and then Regius Professor of Medicine at Oxford. He was passively involved in the spontaneous generation controversy in the 1870s, in which Henry Charlton Bastian, John Tyndall, Louis Pasteur, and others participated. It was widely believed at the time that no form of life could survive a temperature of 100°C for 5–10 minutes. Bastian showed that, in certain organic infusions subjected to this treatment and protected from contamination, living microorganisms might nevertheless develop. He regarded this as evidence of spontaneous generation of life from organic matter. Burdon-Sanderson confirmed Bastian's results, but did not commit himself to an explanation of them. Although Bastian's own explanation was incorrect, he was largely responsible for the general recognition of the extraordinary thermal resistance of spore-forming organisms. On the cholera problem, Burdon-Sanderson went badly astray on two occasions. In 1867 he believed that he had confirmed the impossible claims of C. Thiersch (1856) to have produced cholera in mice by feeding them with filter-papers that had been steeped in choleraic dejections and then dried, and in 1885 he affirmed that "the theory of Dr Koch" was "not supported by any adequate evidence" and was "an unfortunate fiasco".



By courtesy of "The Wellcome Trustees"

some of those who had received the vaccine and whose arms had been made useless by abscesses penetrating to the bone.¹²⁴ Some also developed a fatal septicemia. He later reported that the controversy in Spain over Ferran's claims had "divided the Government and Cortes and formed a capital battlefield", but that the use of vaccine had been prohibited by ministerial decree.¹²⁵ Had this not happened, he adds, "the whole nation would have become Ferranic" at not less than two dollars a head. Some had paid as much as £7 for an injection. Later the ban on the vaccine was lifted.

Sherrington, who had been deputed by the University of Cambridge to investigate Ferran's vaccine while he was in Spain, examined specimens that had been sent at the request of the Spanish government for inoculating soldiers at Aranjuez. He found that they were impure cultures containing many organisms of various kinds, but no comma bacilli. Moreover, the containers of the vaccine "were such as rendered contamination during transit practically unavoidable". Sherrington concluded that Ferran's contentions were "utterly untrust-

worthy". Nevertheless, Ferran persisted in his claims. On 20 August 1888, Pasteur read to the Paris Academy of Science a communication from N. F. Gamaleja of Odessa, who claimed to have developed an anticholera vaccine. Ferran thereupon addressed a memorandum to the Paris Academy claiming priority for his own vaccine.¹²⁶ Both the Royal Academy of Medicine and Surgery of Barcelona and the Section of Hygiene of the Barcelona Medical Congress made formal representations to the Paris Academy supporting Ferran.

In England, Sir J. Fayerer gave in 1888 the annual oration of the Medical Society of London, taking as his subject "The Natural History and Epidemiology of Cholera".¹²⁷ Fayerer was President of the Medical Board at the India Office, a Fellow of the Royal Society and of the Royal Colleges of Physicians and of Surgeons, foreign correspondent and

¹²⁴ *Brit. med. J.*, 1885, 1, 1170.

¹²⁵ *Brit. med. J.*, 1885, 1, 1861.

¹²⁶ Ferran, J. (1888) *Revendication de la priorité de la découverte des vaccins du choléra asiatique*, Barcelona.

¹²⁷ Fayerer, J. (1888) *The natural history and epidemiology of cholera*, London.

member of the Academies of Medicine of Paris and Rome, and a Fellow of the Philadelphia Academy of Sciences. Nevertheless, the views that he expressed on cholera might have been written three centuries earlier. He referred to epidemics of cholera alleged to have occurred in Europe in the sixteenth and seventeenth centuries and said that the disease "is continually present in England, as seen by the Registrar-General's returns". Of "epidemic influence", he declared:

It may depend on certain states of the atmosphere, deficiency or excess of electrical or magnetic tension, different degrees of moisture, of ozone, or other modifications of its physical properties; something propagated in aerial or telluric currents, recurring at intervals, co-operating with local and personal causes, and conferring on the disease its quality of epidemicity; in some cases, perhaps, not only acting as the propagating agent, but as the cause itself.

Fayrer dismissed "theories of contagion and diffusion by human intercourse", and said that there was much to support the view that cholera "is only another form of [malarial] fever", with which it had so much in common "that it is difficult to differentiate between them". Fayrer merely men-

tioned Koch towards the end of his oration, commenting: "I demur to a microbe being accepted as the solution of such a problem as the cause of cholera."

Such were the opinions expressed 33 years after Snow's definitive publication on the mode of communication of cholera, and 4 years after Koch's last report from Calcutta, by one of the most eminent English physicians of his time, who not only held high office but enjoyed an international scientific reputation and had, after completing his medical studies in London as a fellow-pupil of Thomas Henry Huxley, obtained the M.D. both of Rome and of Edinburgh.¹²⁸ Nevertheless, he and others who sympathized with his views were hopelessly out of step with the times. In Germany, Pettenkofer had published in 1887 a massive monograph of over 700 pages on "the present position of the cholera question", declaring this disease to be "the last, surest, hidey-hole [*Schlupfwinkel*] of the contagionists".¹²⁹ For him, he says, a contagionist is one who

¹²⁸ Fayrer, J. (1900) *Recollections of my life*, London.

¹²⁹ Pettenkofer, M. von (1887) *Zum gegenwärtigen Stand der Cholerafrage*, München und Leipzig.



Sir Charles Sherrington (1857–1952) was one of the greatest neurophysiologists of all time, and in 1932 he shared with Sir Edgar Adrian the Nobel Prize for physiology and medicine. His work has been compared in importance with that of such eminent innovators as William Harvey and Ivan Petrovitch Pavlov but, as a young man of 27, he was not so successful in studying the then baffling problem of cholera. In 1885 he went as one of a three-man mission to Spain to study the cholera epidemic there, with special reference to the role of the vibrio and to the value or otherwise of the anticholera vaccine of J. Ferran. The mission concluded that the vibrio probably had some relation to cholera, but was not "the direct cause" of it. Sherrington utterly condemned Ferran's vaccine, in which he found a cocktail of microorganisms that included no vibrios!

believes that an entogenous infective material—by which he meant a material developing in the bodies of the sick—can be transmitted directly or indirectly in an active state from the sick to the healthy.

In this sense, drinking-water theoreticians are full-blooded contagionists. It needs only that a trace of the intestinal evacuations of a cholera or typhoid patient should reach a well or a water-conduit for many people drinking the water . . . to fall sick.

Pettenkofer then gives a detailed commentary on Snow's account of the 1854 cholera epidemic in London. He maintains, correctly, that the epidemic had virtually subsided by the time that the handle of the Broad Street pump was removed, and insists that drinking-water had nothing to do with the epidemic. The most striking and conclusive illustration that Snow had given of his thesis was the case of a Mrs Eley, the widow of the owner of a factory in Broad Street, who lived several miles away in Hampstead. Mrs Eley was partial to the water of the Broad Street pump and had a supply of it delivered daily to her Hampstead home, as a result of which she died of cholera, having had only this indirect connexion with the disease, for there was otherwise no cholera in Hampstead except for Mrs Eley's niece, who had partaken of the same water and suffered the same fate as her aunt. Pettenkofer gives a rather inaccurate account of this incident, retaliating with the extraordinary argument: What if Mrs Eley and her niece had *not* drunk water from the Broad Street pump and had yet died of cholera? The drinking-water theory is, he says, an example of the *post hoc ergo propter hoc* fallacy.

I am sure that all infectious diseases in which drinking-water has hitherto been ascribed a role are originated not by entogenous but by ectogenous infective materials that emanate at certain times from certain localities.

Further on he declares:

It is my innermost conviction that the drinking-water theory has no mightier enemy than bacteriology, which, when it has developed further, will surely free us of the superstition of drinking-water as a source of infection for cholera and typhoid.

It is even believed in England, he adds, that milk churns that have been rinsed with water contaminated by the excrement of the sick can be responsible for the presence of infectious matter in milk. But, the "milk theory is only an extension of the drinking-water theory". Pettenkofer had consistently rejected the "drinking-water theory" for over 30 years, and in 1888 he published another work on "the epidemiological part of the report on the activity of the German Commission sent in 1883

to Egypt and India for research on cholera".¹³⁰ This was the definitive report prepared by Gaffky and published in 1887. Pettenkofer loses no time in making his position clear, declaring in his introduction: "*The whole commission consists of outspoken contagionists and drinking-water theoreticians.*" In England, he says,

almost all doctors since Snow believe that typhoid epidemics are drunk from wells and water-conduits, just as cholera was from the Broad Street pump in 1854

and he approvingly quotes J. Cuninghame as saying that "the whole history of cholera in India negatives the drinking-water theory". If boiling drinking and domestic water could protect against typhoid and cholera, he says, it would be "childishly easy" to prevent epidemics.

But because the origin of epidemics does not lie in drinking-water, it is evident that boiling it does nothing to help.

That specific bacilli are found in cholera and typhoid he does not deny, and for him, he says, there was nothing unexpected in these discoveries. What he had not expected was

the boundless overvaluation of these scientifically very important discoveries in their application and relation to epidemiology, an overvaluation of bacteriology that can hardly last longer . . . Many are so shortsighted as to believe that for the existence of epidemics all that are needed are a specific fungus and susceptible people who are not yet ill, that the major element in prophylaxis is the isolation of the sick and the disinfection of their evacuations, and that all epidemiological experiences and investigations, in so far as they give different results, must be false or useless, that, in a word, epidemiology and the correct prophylactic practice relevant to it only begin with the discovery of bacilli.

Not all bacteriologists were disdainful of Pettenkofer's epidemiological observations and deductions. In 1889, Emanuel Klein, who had five years before been one of the British Cholera Commission in India, published a book on the bacteria of cholera in the preface of which he states that Pettenkofer is "acknowledged to be the greatest living authority on the etiology of cholera".¹³¹ The discovery of the germ of cholera, "which I may at once say has not yet been made", would not in any way alter "the general laws of sanitary science". It would, however, help to answer two "essential questions" on which opinion was still very divided. How did the cholera germ enter the body, and what was the "mode of its exit"? If Koch's contentions

¹³⁰ Pettenkofer, M. von (1888) *Der epidemiologische Theil des Berichtes über die Thätigkeit der zur Erforschung der Cholera im Jahre 1883 nach Ägypten und Indien entsandten deutschen Commission*, München und Leipzig.

¹³¹ Klein, E. (1889) *The bacteria of Asiatic cholera*, London.

had been correct, the prophylaxis of cholera would have been simple.

Acceptance of the correctness of Koch's explanation of the etiology of cholera was therefore very far from universal in the years before the seventh International Sanitary Conference, which opened in Venice on 5 January 1892. Austria-Hungary had taken the initiative in proposing that the conference should be held and Italy had agreed to be host to it. Austria-Hungary had also taken special measures to encourage the participation of an ever-reluctant

Britain; in a letter of 27 November 1891 its ambassador in London had assured the British Prime Minister, the Marquis of Salisbury, that, as promised, his Government "would endeavour to exclude from discussions at the Conference everything that might seem unacceptable to English interests".¹³² Moreover, in preparation for the conference Austria-Hungary had in the previous July

¹³² Great Britain. Secretary of State for Foreign Affairs (1892) *Correspondence relating to the Conference held in Venice in January 1882 respecting the Sanitary Regulations of Egypt*, London.

Zum
gegenwärtigen Stand
der
Cholerafrage.

Von
Max v. Pettenkofer.

(Mit vier Tafeln.)

München und Leipzig 1887.
Druck und Verlag von R. Oldenbourg.

As long ago as 1854, Pettenkofer had denounced the "drinking-water theory" of the epidemiology of cholera. Thirty-three years later he published this massive monograph of over 700 pages in which he repeats and elaborates all the arguments against the idea of water-borne diseases upon which he was to continue to insist until his death 14 years later. In this book, Pettenkofer tries to demolish the impeccable epidemiological research of John Snow and rejects Robert Koch's explanation of the etiology of cholera. It is Pettenkofer's most complete statement of his erroneous doctrine, and a classic of fallacious scientific reasoning. In it, Pettenkofer proclaimed his "innermost conviction" that the drinking-water theory had "no mightier enemy than bacteriology".

National Library of Medicine,
Bethesda, Md., USA

signed a protocol with Britain, to which it invited the other Powers represented at the conference to adhere. This protocol provided that "English ships destined for a port of the United Kingdom, whether infected or not, shall be free to traverse the Suez Canal in quarantine." Ships that were infected or suspect were to be boarded for the whole passage through the Canal by two sanitary guards, whose function was to prevent any contact of persons or goods with the shore. In addition, the Sanitary, Maritime, and Quarantine Council of Egypt was to notify by telegram authorities or ports nominated by each of its members that an infected or suspect ship was in transit through the Canal, the cost of the telegrams being met by the ship concerned. Invitations to participate in the Venice conference had been sent only to those countries represented in the Sanitary Council, and there were therefore only fourteen delegations.¹³³

At the beginning of the conference several delegations suggested that the discussions should cover not only cholera but also plague and yellow fever, but Germany and Spain had instructions from their governments that referred only to cholera and, in the event, this was the only disease discussed, the fundamental issue being the nature of the control measures that should be imposed on westbound British shipping traversing the Suez Canal. Collateral issues were the reorganization of the Sanitary, Maritime, and Quarantine Council of Egypt (hereafter referred to as the Sanitary Council of Egypt) and the sanitary control of the Mecca Pilgrimage.

Commenting on the opening of the conference, the *Lancet* lamented that:

So many incidental interests are involved in anything relating to the Suez Canal that science can hardly be expected to find itself paramount in any conclusions that may be arrived at.¹³⁴

The *Lancet's* Italian correspondent expressed fears about the effects of "French anglophobia" on the outcome of the conference.¹³⁵ The fears proved to be not entirely unfounded, for France—represented by Camille Barrère, still to be the senior delegate of France 46 years later at the last International Sanitary Conference in 1938, Adrien Proust, sole survivor of the participants at the 1874 conference, and P.-C.-H. Brouardel, Dean of the Faculty of Medicine of Paris—took immediate exception to the terms of the Anglo-Austrian protocol, although there is no reason to suppose that its attitude was animated by any wish other than to safeguard southern Europe from the importation of cholera. Spain was more cautious, asking what exactly was

comprised in the term "United Kingdom". For example, did it include Gibraltar? To this question the reply was given that neither Gibraltar nor Malta was included, but only the ports of England, Scotland, and Ireland.

The French case was that much more stringent precautions were necessary for the protection of Egypt and, hence, the Mediterranean ports of Europe. Ships traversing the Red Sea that had had cholera on board within less than 8 days but had neither a doctor nor steam sterilizing equipment on board should be stopped at the Wells of Moses,¹³⁶ any cholera patients being isolated in a special hospital and the healthy passengers disembarked and "isolated in as small groups as possible" for 5 days. In the meantime, their dirty linen and personal effects, and also those of the crew, were to be disinfected, as was the ship. If the ship had a doctor and sterilizing equipment on board, it might, at the discretion of the health authorities, be allowed to proceed through the Canal in quarantine before the expiration of 5 days.

The British case was, as it had been in 1885, that no useful purpose was served by disembarking passengers, even those afflicted with cholera, and certainly not healthy passengers, if the ship was proceeding directly to a port in the United Kingdom. Britain pointed out that cholera had never been imported into the British Isles by sea from India and that the procedure of medical inspection on arrival, isolation of suspicious cases, and medical surveillance of all other passengers offered all the safeguards necessary. To this, a French delegate replied that the situation was now much more favourable than in 1885. At that time,

the discovery of the bacillus of cholera by Dr R. Koch was recent and uncertain. Today, so many observations have confirmed it that it is no longer discussed.

Sterilizers, he continued, had hardly made their appearance in 1885. Today they had been functioning for several years. "Thus, we know the pathogenic germ and the means of destroying it. Why should we not destroy it?" England was surrounded by the sea, which was a first line of defence. It also had an excellent sanitary organization. "But not all countries can spend like rich England." For a majority of countries, quarantine was the only effective safeguard, and the Anglo-Austrian proto-

¹³³ Austria-Hungary, Belgium, Denmark, France, Germany, Great Britain, Greece, Italy, the Netherlands, Portugal, Russia, Spain, Sweden/Norway, and Turkey.

¹³⁴ *Lancet*, 1892, 1, 95.

¹³⁵ *Lancet*, 1892, 1, 110.

¹³⁶ A large oasis, with springs, wells, and date palms, near the north-eastern shore of the Gulf of Suez approximately 10 km from Port Tewfik, and the site of a quarantine station.

col left Egypt and Europe defenceless. The British proposals offered no protection against a false declaration by a master of a ship. Moreover, in the event of bad weather a ship might be obliged to make for the nearest intermediate port. Belgium then pointed to the panic that would be created by the "terrible announcement" that cholera was passing through the Canal and was about to traverse the Mediterranean; Belgium was supported by Turkey, the Turkish delegate adding that in any case the whole system could be nullified by a ruptured telegraph cable. Further, was it really possible, he asked, to compare, from the sanitary point of view, Spain, some Italian provinces, the Midi of France, Greece, and the Ottoman Empire with England, which in the last 30 years had spent 2000 million francs on sanitary improvements?

Egypt pointed out that the French proposals implied disembarking all the passengers, whether healthy or sick. But what would happen in the case of a ship with 1500 persons on board? The accommodation and surveillance of such a large number would place an intolerable burden on Egypt. Only the sick should be disembarked and hospitalized, the remaining passengers being allowed to proceed on their journey.

The discussion continued, the same conflicting points of view being exposed, but at the ninth meeting on 23 January the chief French delegate, Barrère, announced that in private discussion Britain and France had arrived at an "almost complete agreement". The French had modified their proposals, dividing ships into three classes: (1) clean ships (*navires indemnes*); (2) suspect ships (*navires suspects*); and (3) infected ships (*navires infectés*).

The first, having been certified as "clean" by a medical inspection before entering the Canal, would be allowed to proceed without further formalities. Ships that were "suspect" were those that had had cholera on board but no new case for 7 days. These, and "infected" ships (those that had had a new case of cholera within 7 days), were to be subjected to varying degrees of quarantine and disinfection measures according to whether or not they had a doctor and a sterilizer on board. The British still had several reservations, but after further discussion the President was able to declare that the only remaining point at issue was whether or not infected or suspect British troopships should be able to traverse the Canal in quarantine, on which point Britain was supported by Austria-Hungary, Germany, and Italy.

The conference then discussed the reorganization of the Sanitary Council of Egypt and the sanitary control of the Mecca Pilgrimage. By 26 January, the President, summing up the debates, was able to

declare that agreement had been reached on all but two points: the passage of troopships through the Canal in quarantine, and the number of Egyptians who should be members of the Sanitary Council of Egypt. Two days later the conference voted on the first of these questions, and the British amendment to French proposals—which would have permitted infected troopships and passenger ships to traverse the Canal in quarantine—was defeated by 10 votes to 4.

On 30 January the conference met for the signing of a convention, the text of which was that of a French draft as amended in the course of the discussions, it being provided that the signatures should be ratified within not more than 6 months. Five delegations—Austria-Hungary, France, Italy, the Netherlands, and Russia—signed without reservations, and 6 *ad referendum*. The British delegation declared that it was "not yet sufficiently clear as to certain practical consequences" of the convention and therefore could not sign it, the Danish delegate stated that he had not been vested with the power to sign, and the delegation of Sweden/Norway did not attend the meeting. The conference decided that the protocol of the convention should remain open for signature for 4 months, and it was ultimately signed and ratified by all participants.

After the conclusion of the conference, the British decided that the concessions offered by France did not go far enough, and there were exchanges of correspondence between Britain, Austria-Hungary, and France that led to a meeting in Paris from 19 May to 9 June 1892. At this meeting agreement was reached on considerable modifications of two of the articles of the draft convention. It was also agreed that Austria-Hungary should communicate to the other Powers that had participated in the conference the revised texts of the Articles concerned, recommending that they be approved. It was this amended version that was ratified by all participants—thereby becoming the first international treaty relating to health protection. And what was important scientifically was that all participants accepted that the following text should be inserted as a "Nota" at the head of an annex to the convention on "instructions against cholera":

The germ of cholera is contained in the digestive tracts of patients; its transmission is effected principally by the dejections and vomited matter and, consequently, by linen, clothing, and soiled hands.

That such a declaration should have been generally accepted and that the conference resulted in the first International Sanitary Convention are landmarks in the history of international cooperation in matters of the public health. On 31 January the

CONVENTION.

Sa Majesté l'Empereur d'Allemagne, Roi de Prusse; Sa Majesté l'Empereur d'Autriche, Roi de Bohême, etc., etc., etc. et Roi Apostolique de Hongrie; Sa Majesté le Roi des Belges; Sa Majesté le Roi d'Espagne et, en son nom, la Reine Régente du Royaume; Son Excellence le Président de la République Française; Sa Majesté le Roi des Hellènes; Sa Majesté le Roi d'Italie; Sa Majesté la Reine des Pays-Bas et, en son nom, la Reine Régente du Royaume; Sa Majesté le Roi de Portugal et des Algarves; Sa Majesté l'Empereur de toutes les Russies;

Désirant procéder à la réforme du système sanitaire, maritime et quarantenaire actuellement appliqué en Egypte à la navigation, et aussi pour introduire les modifications reconnues nécessaires dans la composition, le fonctionnement et le règlement du Conseil sanitaire, maritime et quarantenaire d'Egypte, ont nommé pour leurs plénipotentiaires, savoir:

These are the opening words of the first International Sanitary Convention to come into force. This convention was the first tangible fruit of seven international conferences spanning 41 years. The seventh conference, of which this convention was the outcome, was concerned only with cholera and, more specifically, with the sanitary control of westbound shipping traversing the Suez Canal, most of which was British. Continental European countries were deeply concerned that the canal might be a conduit for the importation of cholera from India to Europe. History has proved these fears to have been entirely groundless but, in the circumstances, Great Britain and British India (which had separate votes) sometimes found themselves in a minority of two against all other voting countries. Their names are conspicuously absent from the list of countries originally adhering to the convention. But after the conference Great Britain engaged in negotiations with Austria-Hungary and France, winning concessions that were followed by its ratification of the convention.

conference held a brief closing session, with the usual exchange of compliments.

It had required seven International Sanitary Conferences and 41 years for the Powers to agree on a treaty of very limited scope governing maritime quarantine regulations relating only to cholera and only to westbound shipping from the East. However, the convention also provided that the Sanitary Council of Egypt should prepare compatible provisions in respect of plague and yellow fever—two diseases whose etiology and epidemiology were entirely unknown. It also provided that the Council should be reorganized, the number of Egyptian delegates being reduced from 9 to 4, and that all delegates should be required to be physicians or at least diplomats not below the rank of vice-consul.

There were also special provisions referring to the Mecca Pilgrimage.

In retrospect, it is not easy to see much justification for the apprehensions of most of the continental European Powers that cholera might be transported to Europe via the Suez Canal from India or beyond. In just under a quarter of a century of the Canal's existence this had never happened, although the insanitary, overcrowded, and often unseaworthy pilgrim ships traversing the Indian Ocean and the Red Sea were a major factor in bringing cholera to the Middle East. As Koch pointed out two years later, cholera had normally reached Europe overland, and a preoccupation with maritime quarantine precautions was unrealistic.

The eighth conference: Dresden, 1893

From the winter of 1885–86 Europe had been free from cholera, except for a few isolated cases in Italy and France. Whereas the whole of the discussions of the Rome and Venice International Sanitary Conferences had centred on averting the threat of seaborne cholera via the Suez Canal, a serious epidemic that struck Europe in 1892 came by land. Britain—until then supposedly the villain of the piece because of its extensive maritime intercourse with India—was not affected by it, although taking no special precautions. The epidemic first declared itself in Afghanistan and Persia, and then moved westward to Baku, Moscow, and St. Petersburg. Paris was affected, and there was a particularly severe epidemic in Hamburg. Koch, who published extremely detailed statistics of this epidemic, quoted a total of 16 956 cases and 8605 deaths.¹³⁷

There was still no unanimous agreement on the validity of Koch's explanation of the disease. In London, the Royal College of Physicians reported to the Local Government Board in 1892 that cholera was "not, in the ordinary sense of the term, contagious".¹³⁸ It was "certain that physical and moral depression favour the reception and development of the disease" and that, therefore, "apprehension should be allayed, confidence encouraged". It was also especially important to avoid "the frequent use of alcoholic or any stimulants". At about the same time, *Lancet* editorials¹³⁹ echoed the views of Pettenkofer and his fellow localists that dirty immigrants "may provisionally be regarded as many minute migrating fragments of the locality whence they came", and stated that "the purity of the water consumed, of the air breathed, and of the soil can and do prevent the extension of the disease". At a meeting of the Medical Society of London on 5 December 1892, Surgeon-Colonel J. B. Hamilton "asserted, on the authority of an eminent bacteriologist, that cholera had never been proved to be one of the diseases conveyed by bacilli". The air, "plus heat and moisture", constituted "the chief factor of progression".¹⁴⁰ However, the *British Medical Journal*, the editor of which was Ernest Hart, a vociferous supporter of Koch, stated:¹⁴¹

The recent progress of bacteriological research has, however, gone a long way towards justifying Koch's original estimate of the importance of the cholera vibrio . . . it must be admitted that there is now sufficient evidence to justify us in concluding that Koch's cholera microbe is the cause of cholera.

In most countries, the tide of opinion was turning in favour of Koch. In Russia, N. Gamaleja had early accepted Koch's doctrine and had for some years been developing an anticholera vaccine. In France, disbelief was no longer expressed by the workers at the Institut Pasteur, who, still working in the prestigious aura of Pasteur himself, authoritatively represented French scientific opinion. But in Austria-Hungary, the influential Professor A. Drasche of Vienna still remained unconvinced that the comma bacillus was the sole etiological agent.¹⁴² In Germany, Koch himself and his collaborators at the Kaiserliches Gesundheitsamt¹⁴³ represented the official medical science of his country, but Pettenkofer and the substantial number of his followers still obstinately repudiated the idea that the comma bacillus alone could, without undergoing some mythical metamorphosis, be the cause of cholera. On 12 November 1892, according to Koch the day of the last—but not a fatal—case of cholera in Hamburg, Pettenkofer delivered to the Munich Medical Society a long disquisition on cholera, "with special reference to the recent cholera epidemic in Hamburg".¹⁴⁴ The onerous regulations enforced at the time of this epidemic, says Pettenkofer, served, as did the military cordons and isolation of more than 60 years before, to calm those who believed

that cholera is simply an infectious or contagious disease, propagated from man to man, from the sick and their excrements to the healthy, and that the disease poison is eaten and, especially, drunk in water.

¹³⁷ Koch, R. (1896) *Arbeiten aus dem Kaiserlichen Gesundheitsamt*, 10, Anl. 2, p. 26.

¹³⁸ *Lancet*, 1892, 2, 672.

¹³⁹ *Lancet*, 1892, 2, 592, 682.

¹⁴⁰ *Lancet*, 1892, 2, 1331.

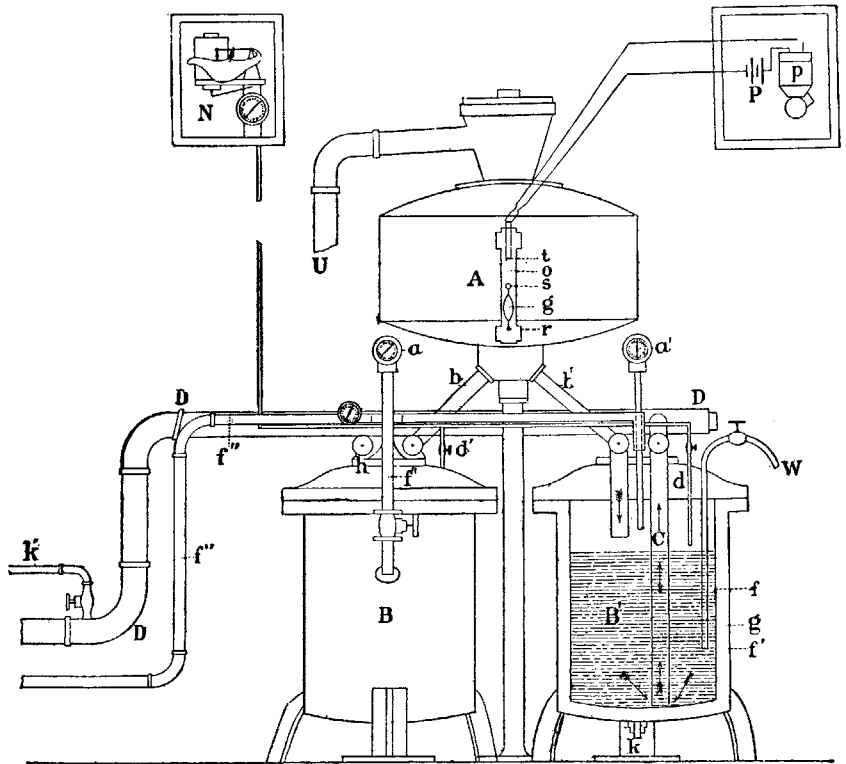
¹⁴¹ *Brit. med. J.*, 1892, 2, 595.

¹⁴² Drasche, A. (1894) *Über den gegenwärtigen Stand der bacillären Cholerafrage und über diesbezügliche Selbstinfektionsversuche*, Wien.

¹⁴³ Later known as the Reichsgesundheitsamt.

¹⁴⁴ *Münch. med. Wschr.*, 1892, 39, 807.

This rather elaborate engine is not, as might be supposed, a miniature atomic-energy plant for the home, but an apparatus for boiling the excrement of cholera patients in order to disinfect it. It was installed in the Alexander Hospital at St Petersburg, which in the summer of 1892 was given over entirely to cholera patients. The illustration is from a book on the 1892 cholera epidemic in Russia by Frank Clemow, which was printed in English in 1893 by the printing office of the Imperial Academy of Sciences, St Petersburg. Clemow explains that the drains opened "into the canals which intersect every part of the city", and that the canals communicated directly with the river Neva. The material to be treated was first placed in the upper receptacle (A), which contained about 18 gallons. It then flowed into the two boilers B and B', which had double walls capable of resisting a pressure of seven atmospheres. Superheated steam was admitted to the space between the two walls at a pressure of three atmospheres, and after about an hour the treated matter was drained away. In the meantime, fresh material—which was doubtless not lacking, for as many as three hundred patients were under treatment at a time—had been placed in A, and the whole cycle was repeated. Clemow states that in the 1892 epidemic there were 555 010 cases of cholera in the Russian Empire, with 267 880 deaths—giving a mortality of 48.2%.



From original in the author's possession

Koch's discovery of the cholera bacillus, he conceded, was a highly interesting and important one, but most people disregarded the large series of epidemiological facts that spoke decisively against a simple contagiousness of cholera. Pettenkofer reiterated his belief that three factors— x , y , and z —were involved in the cholera process. However, z was no longer $x + y$, but "individual disposition", while y was temporospatial (*zeitlich örtliche*) disposition. Contagionists of the Koch school, he says, believe that only x and z are necessary to explain cholera. However, this facile and easily understandable explanation "corrupts all those who have been concerned only with individual cases of cholera and not, as is the epidemiologist, with many cholera epidemics". Dismissing the significance of alleged experimental infections in animals, Pettenkofer states that only on men can an incontestable, unexceptionable experiment be made. He then recounts how he swallowed on 7 October, in the presence of witnesses, 1 cm³ of a broth culture of cholera vibrios prepared from an agar culture provided by Gaffky, after neutralizing his gastric

juices with a solution of sodium bicarbonate. He estimated that his "cholera drink" contained a thousand million vibrios but was not pessimistic about the outcome, "because I was firmly convinced that x could not do away with me without my y ". The result of this experiment was that from 9 October onwards Pettenkofer experienced borborrygmi, some diarrhoea, and some colic. He continued to consume his usual amounts of food and drink, and his symptoms slowly subsided. On the morning of 15 October he had a normal stool and thereafter had no further symptoms. He had rejected the earnest advice of a colleague to treat himself with calomel or tincture of opium. Pettenkofer's colleagues, Pfeiffer and Eisenlohr, had been harvesting his stools for bacteriological examinations, and they found in the more watery specimens a "pure culture" of vibrios. But from 15 October no more vibrios were to be found. On 17 October, Pettenkofer's disciple, R. Emmerich, performed a similar experiment upon himself, passing a stool almost hourly for 43 hours.

These two experiments in man, claimed Petten-

kofer, showed "that the living comma bacillus in the intestine does not produce the specific poison that results in cholera". Koch and his followers might say that he and Emmerich had had mild attacks of cholera. "I am glad to give my adversaries this pleasure, but on epidemiological grounds I cannot accept that x and z suffice for cholera epidemics without any y The fear of the comma bacillus is quite futile; it leads only to measures that cost much trouble and money." In the discussion that followed this address, Emmerich stated that Pettenkofer's original intention had been to try his experiment on 50-100 of his pupils.¹⁴⁵ However, the two experiments that had been carried out sufficed to show that the comma bacillus could not produce cholera, but only a cholera-like diarrhoea. Pettenkofer's demonstration of the dependence of cholera on temporospatial conditions, he said, at a time when hygiene and bacteriology were in their infancy, or had not even been born, was a work of genius:

If we have hitherto honoured von Pettenkofer as the great immortal investigator and teacher, we must henceforth extol him as one of the heroes of science who, like a champion, wagered his life for the recognition of truth.

Emmerich was followed by Professor H. Buchner, who congratulated Pettenkofer on his "wonderful experiment", which proved that the cholera vibrio could only produce x . It must be concluded that an unknown further condition, a something, for the real cholera process, had been lacking. That this something, this y , was produced and delivered up by the soil was beyond doubt. Closing the discussion, Pettenkofer expressed the hope that now that the x was known, the two other unknown quantities [y and z] would soon be found by the bacteriologists, so that a sure protection against cholera would become possible. The meeting ended with long and sustained applause.

Reactions, both in Germany and abroad, to Pettenkofer's experiment on himself were mixed. There was general approval of his courage, but much doubt, or positive disbelief, about the validity of his conclusions. The *Münchener medizinische Wochenschrift* reported mixed reactions in the German and Austrian medical press. The *Gazette médicale de Paris* published an extensive summary of his paper but made no comment on it. The *Lancet* published an almost complete version of it in English and a leader underlining the differences of opinion on the etiology of cholera. The *British Medical Journal*, on the other hand, published a short summary and a highly sceptical leader. A leader in the *Journal of the American Medical Association* expressed the same scepticism.

In the following year, Elie Metchnikov reported a similar experiment on himself in which, after first neutralizing his gastric juices with sodium bicarbonate he swallowed an emulsion of part of a culture of a vibrio from Hamburg in sterile broth.¹⁴⁶ His laboratory technician, Latapie, made the same experiment. Neither had any symptoms, nor could they discover vibrios in their stools. A week later, they both repeated the experiment, but both suffered no worse result than borborygmi and a slight malaise on the sixth day. On that day they both swallowed part of a culture of vibrios, as also did a third person identified only as "Gr.". During the next few days, both Metchnikoff and Latapie had a tendency to constipation, the latter developing a slight diarrhoea on the ninth day. In the stools of neither were vibrios detectable. Gr., on the other hand, had frequent loose stools that gave on gelatine plates "only a pure culture of comma bacilli", but after six days he was again "absolutely normal". Metchnikoff cites a number of other examples of experimental infection in human subjects, including those initiated by Hasterlik of Vienna, and from these and his own observations he draws the conclusion that:

It is no longer Koch's theory that should adapt itself to the facts of epidemiology, but the facts that should be reconciled with the fundamental truth that the comma bacillus is the specific agent of Asiatic cholera.

By 1894, Drasche of Vienna was able to cite 27 experiments on themselves by 21 different persons, of which 10 had been positive in the sense that varying degrees of diarrhoea had resulted, and 17 had been negative.¹⁴⁷ In most of the positive cases and a few of the negative, comma bacilli had been found in the stools. Drasche concludes: "With the results of the auto-infection experiments the bacillary cholera question is not settled."

In 1897 P. Hauser—a corresponding member of important medical societies or academies in Paris, Bordeaux, London, Lisbon, and Madrid—published a monograph of over 500 pages on cholera in Europe.¹⁴⁸ All now agree, he says, that cholera is caused by a specific germ. Some consider that drinking-water is the principal vehicle of transmission. Others, that the soil is the true culture medium of the germ, which is transmitted to man by food and drink that have been in contact with contaminated air. Hauser is as scornful of "la doctrine

¹⁴⁵ *Münch. med. Wschr.*, 1892, 39, 827.

¹⁴⁶ *Ann. Inst. Pasteur*, 1893, 7, 562.

¹⁴⁷ Drasche, A. (1894) *Über den gegenwärtigen Stand der bacillären Cholerafrage und über diesbezügliche Selbstinfektionsversuche*, Wien.

¹⁴⁸ Hauser, P. (1897) *Le choléra en Europe depuis son origine jusqu'à nos jours* . . . , Paris.

hydrique" as Pettenkofer of the "drinking-water theory":

The clinical facts assembled by medical epidemiologists, in France as in Germany, are in disagreement with Mr Koch as regards the constant presence of the comma bacillus in the dejections of cholera patients and the preservation of its toxic properties outside the human organism.

Koch as a bacteriologist had, he says, concerned himself only with laboratory studies of the germ, and had not taken into consideration individual disposition, local disposition, meteorological and seasonal elements, and the hygienic conditions of individuals and localities. Drawing directly opposite conclusions from those of Metchnikov himself, Hauser states that Metchnikov contributed "to ruin M. Koch's edifice and to demolish the basis of the drinking-water doctrine". And, he continues, "we are convinced that the time is not far off when everyone will recognize that the etiology of cholera is very complex and cannot be confined within the too restricted formulation of a hydrous origin." A little further on, he refers to the "deceptive charm of the hydrous doctrine".

Thus, on the eve of the twentieth century there were still those who could not accept what Snow had demonstrated over 40 years before from epidemiological studies, and what Koch had confirmed by other means—his microscope and culture media—some three decades later. The pioneer work of Pacini had been entirely forgotten.

As regards the prophylaxis of cholera, there was general scepticism about the alleged vaccine developed by Ferran in Spain. In Russia, Gamaleja had simultaneously been working on a vaccine, and in France, W.-M. Haffkine at the Institut Pasteur in Paris enhanced the virulence of the cholera "virus" by intraperitoneal passage through guinea pigs, attenuated it by aerobic culture in broth, and claimed that it protected guinea pigs, rabbits, and pigeons against experimental infections.¹⁴⁹ Gamaleja and Haffkine were both to have medical research institutes named for them—the first in Moscow and the second in Bombay—but the efficacy of the anticholera vaccines that they developed is a matter for some doubt.

When the eighth International Sanitary Conference opened in Dresden on 11 March 1893, Robert Koch was again a member of the German delegation. In the Belgian delegation was E. van Ermenegem, a well-known bacteriologist and supporter of Koch. Barrère, Brouardel, and Proust—a powerful and experienced trio—represented France, and Thorne Thorne was again the medical delegate for Britain. Nineteen countries, all of them European, were represented, and 5 of them sent only diplomat-

ic delegates.¹⁵⁰ Austria-Hungary had again taken the initiative for convening the conference, and again the sole disease under discussion was cholera. In preparation for the conference, Austria-Hungary had circulated to participating governments a questionnaire referring to the definition of infected and suspect localities, the precautions to be taken in respect of railway and postal communications, and the sanitary control of travellers by land and sea. In an introductory address, the first Austro-Hungarian delegate, Hengelmüller de Hengervár, referred to the serious interference with international commerce and the inconvenience to travellers that had been occasioned by the restrictive measures adopted during the cholera epidemic of the previous year, which were not "justified by the requirements of a sanitary service based on the results won by modern science". He hoped that the present conference would be able to accomplish for other arteries of communication what the Venice conference had for the sanitary control of traffic through the Suez Canal. A German diplomatic delegate then spoke of the disastrous effects on German trade that had resulted from excessive measures against the importation of German goods during the Hamburg epidemic. He proposed that the conference should confine its discussions to cholera but that it should exclude all questions relating to the importation of the disease by sea from the East, for which such a satisfactory solution had been found by the Venice conference. Maritime quarantine, he added, should be replaced by a system of medical inspection. The chief Russian delegate then drew particular attention to the need for the sanitary regulation of international traffic on the Danube, and was followed by the Italian medical delegate, who declared that it would be superfluous to discuss "the various scientific theories on cholera". Thorne Thorne then described in some detail the system of medical inspection adopted at British ports, and stated that in the previous year there had been 29 imported cases of cholera in Britain, none of which had given rise to an outbreak of the disease. No one had been refused admission to the country except some "very poor Jews" coming from Russia, and this was only because they could not meet the legal requirement to state the address to which they were going. Britain, said Thorne Thorne, had not rejected the quarantine system in the belief that cholera was not transmissible from man to man.¹⁵¹ On the contrary, "the public health service of the United Kingdom is

¹⁴⁹ *C. R. Soc. Biol. Paris*, 1892, 44, 633, 671.

¹⁵⁰ Denmark, Montenegro, Portugal, Russia, and Sweden/Norway. The other countries were Austria-Hungary, Belgium, France, Germany, Great Britain, Greece, Italy, Luxembourg, the Netherlands, Romania, Serbia, Spain, Switzerland, and Turkey. The chief delegate for Austria-Hungary acted also as the delegate for Montenegro.

¹⁵¹ This was hardly an accurate statement, if considered historically.

in perfect harmony with the scientific opinion of the great nations represented at this conference." This declaration, made on 17 March 1893, was the first explicit and official adherence of the British to the contagionist school, but did not in any way imply a weakening of British opposition to quarantine.

The conference appointed three committees to study particular questions in detail: (1) notification of cases of cholera and internal measures; (2) external measures on land, on inland waterways, and at sea; and (3) the sanitary regulation of the mouth of the Danube in the Black Sea at Sulina. The conference held 12 plenary sessions, most of which were devoted to discussing the reports of the committees, on which there was little disagreement. By the tenth session, all questions of substance had been settled and it remained only to agree on a final protocol. The chief delegate of Austria-Hungary pointed out that although the conference had been a purely European one its decisions were of importance beyond the Atlantic, and especially to "that great nation, the Republic of the United States". He therefore requested that the conference proceedings be communicated to the United States Government. In this he was seconded by Barrère of France, who proposed that a similar course be taken with the countries of South America and also, through the British Government, with Cyprus, Gibraltar, and Malta. The Italian delegate then proposed that Canada should also be included, and all these motions were accepted unanimously. The new con-

vention elaborated by the conference was signed by only 10 of its members, Britain, Denmark, Greece, Portugal, Romania, Serbia, Spain, Sweden/Norway, and Turkey all announcing that they would have to refer it to their governments. The conference held its closing session on 15 April. The governments signing the convention pledged themselves to notify each other urgently of any outbreaks of cholera within their territories and agreed that the only goods to be subject to import restrictions were used clothes and bed linen and rags, which were to be either prohibited or disinfected, but not retained in quarantine. It was specified that letters, newspapers, and books should be free from all restrictions. Travellers by rail could be detained only if they had cholera or cholera-like symptoms, and there was to be no more land quarantine. The maritime quarantine measures were essentially the same as those adopted at the previous conference, and special measures were prescribed for ships entering the Danube from the Black Sea at Sulina, and especially those from Odessa. Russia had taken the initiative in proposing a relaxation of sanitary restrictions on international traffic on the Danube, but Romania opposed the Russian contentions at great length and pointed out that the contribution of Russian shipping to this traffic was relatively unimportant. Eventually it was agreed that non-infected ships coming from a cholera-infected port should remain in dock at Sulina for 3 days, during each of which there would be a medical inspection.

The ninth conference: Paris, 1894

On 7 February 1894 the ninth of the International Sanitary Conferences opened—the third to be held within two years. France had convened the conference, and Barrère was elected as its president. In his presidential address he pointed out that the Venice conference had succeeded in agreeing on steps to keep cholera out of Egypt and the Mediterranean, and that at Dresden in the following year the conference had agreed on a system of notification and of maximum precautions to be taken in the event of cholera outbreaks in Europe. It remained now to take the third step—the sanitary control of the Mecca Pilgrimage, which was recognized to be the major factor in the westward spread of cholera. Since the year 1865, Mecca had had no less than 8 cholera epidemics (in the years 1871–1893), the one in 1893 having been particularly severe and cost the lives of thousands of pilgrims. Persia had “paid an even more terrible tribute”. It was therefore not only the Red Sea but also the Persian Gulf that needed to be placed under sanitary surveillance. The epidemics of cholera in Mesopotamia and Syria in 1889, 1890, and 1891 clearly demonstrated the danger of importation of the disease by that route. Barrère was followed by Proust, who in a long disquisition gave a summary of the outcome of previous International Sanitary Conferences since 1851 and insisted on the need not only for sanitary surveillance of the Red Sea and the Persian Gulf but also for adequate precautions to be applied to pilgrim ships at their ports of departure. Several European countries had a direct interest in the Mecca Pilgrimage—Britain because of its Moslem subjects in India, estimated to number 60 million; the Netherlands because of the Moslems in the Dutch East Indies; France because of Algeria; and Russia and Austria-Hungary because of the Moslems in the Asian parts of the Russian Empire and in Bosnia-Herzegovina respectively. The appalling conditions of the pilgrimage are illustrated by the fact—reported by the Austro-Hungarian delegation—that 59 of 120 pilgrims from Bosnia-Herzegovina in 1893 perished of cholera, and the road from Jidda to Mecca was sometimes strewn with the decomposing bodies of those who had been left where they fell to be devoured by wild animals and

birds. According to a report from the French consul at Jidda, presented to the conference by the French delegation, there had been 35 000 deaths within the space of 5 days.

However, according to C. Izzedine, who was then medical officer at Mecca, the total number of deaths of pilgrims during the whole period of the pilgrimage was 30 336.¹⁵² He describes how the epidemic first broke out at Mouna, about 5 km from Mecca, to which it soon spread. Mouna and the road to Mecca were littered with corpses, and in the holy city itself many streets were encumbered with the bodies of victims. Survivors appeared to be in a state of stupor. “It seemed to me that among the mass of pilgrims before my eyes the brain was not functioning any more. It was obvious that the pilgrims were acting as automatons.” Basing himself on the interrogation of old inhabitants of the region, Izzedine fixed the date of the first invasion of the Hejaz by cholera as 1831—which agrees very well with what is known of the march of cholera elsewhere in that year. He estimated that of 200 500 pilgrims in 1893, 15 out of every 100 had perished miserably from cholera. There is no record of the number of pilgrims who died of heat stroke and other ailments.

Sixteen countries participated in the conference, this time including the USA, which sent a delegation of three physicians headed by Dr. E. O. Shakespeare. Koch was not present at this conference, but the Belgian delegation again included van Ermengem and the French, Barrère, Brouardel, and Proust. In 1885, the British Government had made its participation at the Rome conference conditional upon the granting of a separate vote for British India, and early in the course of the conference the chief British delegate asked for a similar privilege for the “special delegate for British India”, Surgeon-General J. M. Cuninghame. This request was only partially granted, Cuninghame being given the right to vote separately in committee but not in plenary session. Also in the British delegation was Thorne Thorne.

¹⁵² Izzedine, C. (1909) *Le choléra et l'hygiène à la Mecque, Paris*.



WHO photograph

The Ka'ba, the central shrine of the Islamic faith, is for Moslems the most venerated spot on earth and is at the centre of the Great Mosque of Mecca. Every year hundreds of thousands of Moslems make the Pilgrimage to Mecca, where they are required to walk seven times round the Ka'ba and to stay in the area for a few days in conditions that are necessarily very overcrowded. The International Sanitary Convention of 1894 was concerned exclusively with the sanitary regulation of the Mecca Pilgrimage. Great Britain was directly concerned because of its estimated 60 million Moslem subjects, France because of Algerian pilgrims, and Austria-Hungary, the Netherlands, and Russia because of their subjects who were of the Islamic faith. Until 1956 measures for the sanitary control of the Pilgrimage were as laid down in provisions of the International Sanitary Regulations, but in that year the World Health Assembly, recognizing that this was essentially a responsibility of the Government of Saudi Arabia, abrogated these provisions.

The conference closed on 3 April and was exclusively concerned with the Mecca pilgrimage, and in particular the precautions to be taken at ports of departure, the sanitary surveillance of pilgrims traversing the Red Sea, and the sanitary regulation of shipping in the Persian Gulf. The United States delegation tried unsuccessfully to persuade the conference to concern itself with the sanitary control of European emigrants to the Americas. Opposing this proposal, the Italian medical delegate stated that in the preceding year four ships that had had a thorough medical inspection had left Naples in an apparently healthy condition; nevertheless, cholera broke out on all of them and the passengers were refused admission at the South American ports for which they were bound. By the time the ships returned to Naples, there had been a total of 522 cholera deaths. The American delegation subsequently made a counterproposal that there should be convened as soon as possible, either at Brussels or the Hague, another International Sanitary Conference to consider the problem of the threat of the

introduction of cholera into the USA by European emigrants, of whom there had been a total of over 6 million in the years 1881–1890. This proposal met with a generally favourable reception but never came to fruition.

The outcome of the conference was a third convention, supplementing those of Venice and Dresden and containing four annexes with detailed provisions. Of the 16 participating countries, 13 signed the convention, the abstainers being Sweden/Norway, Turkey, and the USA. Britain signed with some reservations: it would not agree that pilgrims should be required before leaving to show that they had sufficient means for the return journey; nor that each pilgrim on a ship should have at least 2 m² of space;¹⁵³ and it rejected *in toto* Annex III to the convention, which contained detailed provisions for the sanitary control of shipping in the

¹⁵³ The Italian delegation pointed out that this was the usual allowance for a corpse in a cemetery, but the British dismissed this as irrelevant, adding that the existing allowance of 1.5 m² per person was the same as that on British troopships.



From original in the author's possession

The above is a reproduction of a plate from a work on cholera, published in 1892, by the great French sanitarian and pioneer of international health cooperation, Adrien Proust. It shows pilgrims to Mecca patiently purging their quarantine in a corner of the El Tor quarantine station at the northern extremity of the Red Sea. Proust included this picture to show how encumbered were some of the pilgrims by their personal belongings. Between 1831 and 1895 there were sixteen serious cholera epidemics among the pilgrims, the infection having been imported by those coming from India. The pilgrims came not only from India and further east, but from all corners of the widespread world of Islam, and included subjects of Austria-Hungary and Russia. Pilgrims returning to Europe were regarded as constituting a special threat, and for 75 years the Pilgrimage was subject to international sanitary legislation. The cholera epidemic of the Pilgrimage of 1893 was the worst of them all, costing the lives—according to the estimate of the medical officer at Mecca during that year—of 30 336 out of a total of 200 500 pilgrims.

Persian Gulf—98% of which, according to a statement by the chief British delegate, was British. All the other delegates who signed the convention reserved the right to enjoy also the exemptions claimed by Britain, and the relevant provisions of the convention thereby became a dead letter. A proposal had been made by Austria-Hungary, seconded by the Netherlands, for the reform of the Sanitary Council of Teheran to ensure effective international representation, but this was opposed by both Britain and Russia. The Teheran Council was, in fact, completely ineffectual. It had been created in name after the Constantinople conference of 1866 and consisted of a group of Persian physicians, most of them trained in Teheran, under the chairmanship of a Persian dignitary, and on the rare occasions when it met the physicians of the British and Russian legations were also present. Not the least of the Council's handicaps was the lack of a budget, the Persian Government limiting its support to making a room available for meetings. From a financial point of view, Britain had good reasons for opposing a reform of the Council, for in the scheme put forward by Austria-Hungary it would have been responsible for almost one-third of the part of its budget that was to come from sources outside Persia.

A conspicuous feature of the conference was a direct and very carefully prepared attack launched on the British by one of the French delegates, Henri Monod. Surgeon-General J. M. Cuningham, formerly the Sanitary Commissioner for India, was the special delegate for British India and a few years previously had been notorious for his anticontagionist views. Early in the conference he had made a statement stressing the efforts made by the British to improve sanitary conditions in Indian towns. Monod retaliated by pointing out that similar declarations had been made in 1866 by Goodeve in Constantinople, in 1874 by Dickson in Vienna, and in 1885 by Fayrer in Rome. He then produced detailed statistics from official British-Indian publications which showed that from 1878 to 1892 the prevalence of cholera in India, far from decreasing, had undergone a considerable increase, the number of registered deaths having risen from 318 228 in the first of these years to 721 938 in the last. He then concluded:

The factory of cholera is to be found in British India. Europe did not know cholera before India became a British possession. It is therefore principally the British Empire that has the responsibility of opposing its exportation.

In his reply, made over a month later, Cuningham spoke of the role played by "the presence or absence of that mysterious power about which we

know so little and that we designate by the name epidemic influence". He then challenged Monod to quote health statistics for Algeria and Tonkin, adding that even in France such statistics were available only for towns of over 5000 inhabitants. Monod did not take up this challenge but said that Cuningham, in speaking of "the mysterious power", had "touched on a scientific field in which I have not the competence to follow him". But Cuningham was not the only participant still under the influence of localistic ideas of the etiology of cholera. The medical delegate of the Netherlands, W.-P. Ruysch, described the sanitary precautions required of pilgrims leaving the Dutch East Indies in order to avoid their bringing Pettenkofer's *x* with them, and expressed the hope that the conference would find a means to combat also *y* and *z*. These were the only occasions when the conflicting ideas of the etiology that still prevailed were reflected in the discussions at the conference.

During this 1894 conference, only two statements—those of Cuningham and Ruysch—had a bearing on scientific theories of the etiology of cholera, and both of them reflected views that were compatible with Pettenkofer's doctrine. In the same year Pettenkofer himself published a retrospective analysis of cholera and typhoid outbreaks in Munich, concluding that it was never possible to find that either disease depended on water "in the sense of the contagionist drinking-water theoreticians".¹⁵⁴ Referring to the absence of cholera from England since 1866 despite the lack of quarantine, he said that it was very desirable that in Germany also the localistic rather than the contagionist doctrine should be followed and that "personal freedom, trade, and travel" should not be needlessly oppressed. In March 1894 Pettenkofer delivered an address to the Munich Medical Society on "cholera explosions and drinking-water", which he began by referring to an epidemiological study published by Koch on cholera in Germany during the winter of 1892-93.¹⁵⁵ Koch, he says, draws the conclusion that explosive outbreaks of cholera originate from drinking-water and can be explained only by the "drinking-water theory". He admits that this theory is now the "reigning belief" but then proceeds to reason on epidemiological grounds that it is unfounded. The contagionists boasted that they had limited the spread of cholera in Germany by "zealous comma-hunting, isolation, and good water-filters". He declares that, "as a good German", he hopes from the bottom of his heart that these gentlemen are right, but that in the light of earlier experiences he cannot remain content with this

¹⁵⁴ *Munch. med. Wschr.*, 1894, 41, 181.

¹⁵⁵ *Munch. med. Wschr.*, 1894, 41, 221, 248.

explanation. He concludes by saying that he is no opponent of bacteriology. On the contrary, he believes that this discipline will help to solve the problem of infectious diseases. The object of his discourse, he declares, was to awake among the bacteriologists a belief in the still-unknown γ . That Pettenkofer still had a following not only in his own country but beyond is indicated by the fact that in 1894 he was appointed an honorary member of the Warsaw Society for Military Hygiene.¹⁵⁶

In September of the same year, the Eighth International Congress on Hygiene and Demography took place in Budapest, and among those submitting papers were Carlos Finlay, Gerhard Hansen, Shibusaburo Kitasato, Alphonse Laveran, Friedrich Loeffler, Elie Metchnikov, Ronald Ross, and Emile Roux.¹⁵⁷ Florence Nightingale contributed, by invitation, a paper on "Village Sanitation in India", and the contribution of Sir Joseph Fayrer, then aged 70, was an anachronistic paper on the relation to health of physical and climatic conditions in the same country. Koch and Pettenkofer were both honorary foreign Presidents of the congress, but neither attended nor submitted papers, although the latter's disciple, Emmerich, was present as an official German delegate. John Shaw Billings and W. C. Gorgas also attended, representing the Army and the Navy of the United States respectively. In contrast to the International Sanitary Conferences, the International Congresses of Hygiene were essentially non-governmental—although many governments sent official delegates—and the subject-matter of the discussions was purely scientific. One of the main diseases discussed at the Budapest Congress was cholera, and it is clear that scientific opinion as to its etiology was, ten years after Koch's incrimination of the comma bacillus, still divided. Referring to the congress three years later, Hauser said that the views expressed there by "very distinguished bacteriologists" had seriously shaken "the basis of the hydrous doctrine and supported Pettenkofer's ideas on the temporospatial influence on the genesis and development of a cholera epidemic". In a paper presented to the congress, Professor Max Gruber of Vienna, while not disputing the specificity of the comma bacillus in cholera, expressed his belief that "something else" was necessary, "probably a something that influences either the formation or the absorption of the poison".

We probably do not err when we suspect that the riddle of cholera epidemiology, the known but as yet unexplained dependence of cholera epidemics on place and time, stands in relation to this unknown somewhat.

In the congress proceedings, Gruber's paper is followed by an abstract of a paper by Metchnikov

in which he concludes that antagonism between the cholera vibrio and the intestinal flora is the phenomenon by which the "fundamental truth" that Koch's bacillus is the specific agent of cholera can be reconciled with "epidemiological data, notably the influence of place and time". Commenting on Metchnikov's contribution, Gruber postulated the tortuous theory that the comma bacillus was endemic to Europe but that "a hitherto unknown specific germ" spread from India and, developing in the human intestine, facilitated the action of the endemic vibrio. J. L. da Silva Martins, of the Bacteriological Institute of Lisbon, claimed that the outbreak of "cholera" in that city had been shown to be due to a vibrio other than Koch's comma bacillus. In the discussion that followed, F. Hueppe of Prague stated that, while Koch's comma bacillus was the etiological agent of cholera, his "conception of the specificity and constancy" of its pathogenic properties was untenable, and that Pettenkofer's conception of "temporospatial disposition" must be developed. J. R. Altschul, also of Prague, regarded the day's session of the congress as a "triumph of epidemiology". In the session that followed, Surgeon-General C. A. Gordon spoke from experience of cholera in British India from 1842 to 1879. The causes of cholera, he said, had been variously defined according to the theories prevailing at the time, and these included climatic influence, septic conditions, and "an unknown something". The particular hypothesis of the present time [presumably the comma bacillus] was "but a revival of one of those so enumerated". The relation of contaminated water to cholera was "variously viewed". Some thought that it was a direct, and others only a predisposing, cause. "On the other hand it is considered that the oxidizing effect of water on organic matter is antagonistic to the propagation of cholera by this means." Some who drank contaminated water contracted cholera. Others who drank the same water did not. Later, N. C. Macnamara left no doubt as to his belief in the etiological role of the cholera bacillus but pointed out that there were "men holding most important positions as sanitary advisors to their Government, who I believe still demur to accepting the fact of the specific nature" of the organism. He called for the establishment of an authoritative international committee to advise governments on the nature of cholera and on its prevention. F. Cle-mow, a British physician who practised in St. Petersburg and an unashamed "drinking-water theoretician", then referred to

¹⁵⁶ *Münch. med. Wschr.*, 1894, 41, 279.

¹⁵⁷ *Huitième Congrès international d'Hygiène et de Démographie*, 1896, Budapest.

observers who deny to water any part whatever in the diffusion of cholera, who do not believe that the poison of cholera lies in the dejecta of the patient, and who are prepared to assert that the guarding of water supplies from contamination by dejecta and the use of boiled water during an epidemic may with safety be neglected.

He said that "the clearest exposition of such views" was to be found in a monograph on cholera published by Professor Erismann in Moscow in 1893. But, concluding his paper, he emphasized that there was "strong evidence that local conditions, such as elevation and dampness of the soil, are important factors in the cholera problem". Following Clemow, J. Polak of Warsaw described the cholera epidemic of 1892 in that city, and raised the question of the etiology of cholera—this question being, he said, "the most interesting, the most difficult and, so to speak, the most delicate" of those to be answered. After a long and careful consideration of the facts he concluded that Koch's explanation was an over-simplification and that the basis of "prophylaxis and certainly of efficacious prophylaxis" was to be found in the *x*, *y*, and *z* of Pettenkofer. Ruysch then described cholera in the Netherlands in the years 1892–94, opening his paper with the words: "After bacteriology, epidemiology, after laboratory experiments, experiments on the field of battle." Ruysch contented himself with giving a factual account of the outbreak. "God knows", he said, which of the various theories is correct. The three cholera outbreaks of 1892–94 in St. Petersburg were then described by N. Ivanovsky, who believed that meteorological phenomena could not be exculpated, and pointed out that experienced bacteriologists had not been able to find comma bacilli either in the river Neva or in its tributaries or the canals.

The proceedings of the Budapest congress are of particular interest as reflecting the doubt that still existed in 1894 in scientific circles as to the etiology of cholera and the force that Pettenkofer's doctrines still exerted. There was even a paper in German by an English physician, M. A. Adams, on the relation of diphtheria epidemics and ground-water. In contrast, preliminary reports were independently submitted both by Yersin (through G. Treille) and Kitasato¹⁵⁸ of the isolation in Hong Kong of the plague bacillus and the successful production of experimental infections in animals.

The Budapest congress was followed, also in September 1894, by a meeting at Magdeburg of the German Society for Public Health¹⁵⁹ at which there was a discussion of "the cholera question" in which both Koch and Gaffky participated¹⁶⁰. The first speaker, von Kerschensteiner, stated that the cholera vibrio was now generally recognized as the

causative agent of the disease, but that without the concept of a local, temporal, and personal disposition many epidemiological facts were inexplicable. Gaffky then spoke, confining himself to an outline of preventive measures, and was followed by Koch, who was greeted by loud applause. Koch's tone was conciliatory; until a few years ago, he said, there were wide differences of opinion between North and South Germany (in other words, between Berlin and Munich). Now, however, even Pettenkofer had recognized that the cholera bacillus was his *x*.

The 10-year struggle over the nature of cholera has, I believe, thus come to an end. We are all unanimous that a quite distinctly characteristic parasite is the cause of cholera. When I say this in summary fashion, I do not at all mean that anyone into whose mouth or stomach or even intestine the parasite is introduced will in all circumstances get an identical severe attack of cholera. I have never maintained this. I have from the beginning held the view that, even if we know the specific cause, we must also take into account a whole number of contributory causes that can be characterized as the local, temporal, and individual conditions that must come to the help of the parasite in order to allow a disease to be produced. I thus believe that in this respect we North Germans are unanimous with the South Germans. Differences of opinion exist only in respect of how to conceive these contributory causes and what they are, and on this point I must regretfully confess that we know relatively little.

After a lengthy statement on protective measures against cholera, Koch spoke disparagingly of international efforts to limit its spread. The Dresden conference [of 1893], he said, had not concerned itself with prevention but only with the abolition of unnecessary restraints on travel, while the Paris conference [of 1894] represented an attempt at closing certain portals of entry. It was said that the Red Sea and the Persian Gulf were the most important of these and that both should be under surveillance to prevent the entry of cholera. However, everyone familiar with the history of the disease knew that almost all epidemics came neither via the Red Sea nor via the Persian Gulf, but from the Asian steppes to Southern Russia. Closing the Red Sea and the Persian Gulf, he believed, served no purpose:

I maintain that these international efforts are quite superfluous, for the best international protection would be for each State to do as we do, and to seize cholera by the throat and stamp it out. I would ask that this last thesis be not taken in the sense that such international efforts are of much use to us. (Lively and repeated applause).

¹⁵⁸ Kitasato was mistaken. He had not discovered the plague bacillus, but never admitted his mistake. See: Howard-Jones, N. (1973) *Perspectives in Biology and Medicine*, 16, 293.

¹⁵⁹ Deutscher Verein für öffentliche Gesundheitspflege.

¹⁶⁰ *Berl. klin. Wschr.*, 1894, 31, 967.

Thus did Koch rally to the philosophy of cholera control that the British had tenaciously maintained, not by any means invariably for the right reasons, for over 40 years.

Closing the discussion, von Kerschensteiner thanked Koch for his participation and said that he had only one point of disagreement with him: the value of international meetings. Some of the participating countries could only with difficulty introduce sanitary measures and they must be influenced by such meetings. Here was, for the last decade of the

nineteenth century, a very far-sighted understanding of what is now widely recognized as an important function of intergovernmental meetings on health matters—the stimulus that they furnish to economically less developed countries to improve health conditions internally.

Koch's statement that the 10-year struggle over the nature of cholera was at an end proved to be over-optimistic, and sharp differences of opinion were to persist among "contagionists" and "localists" for many years.

The tenth conference: Venice, 1897

Most of the first nine International Sanitary Conferences were concerned mainly with cholera. At the first and second, in 1851 and 1859, the discussions on cholera were concentrated upon whether or not its spread could be controlled by maritime quarantine measures and *cordons sanitaires* and whether, therefore, it was a suitable subject for international consideration. At all the succeeding seven conferences—except the fifth, which also discussed yellow fever and took place in unique circumstances having little or nothing to do with those of the other conferences—cholera was the sole disease considered.

As from the ninth conference, the etiology and mode of transmission of cholera were no longer an issue at the intergovernmental level, although differences of opinion still prevailed as to the most appropriate administrative measures for the control of the disease, and in particular the feasibility of exercising control over healthy carriers of the vibrio. Outside the framework of the conferences, Pettenkofer and his disciples obstinately continued a rearguard action against the concept that cholera and typhoid could be transmitted by water.

The tenth International Sanitary Conference, which opened in Venice on 16 February 1897, set a precedent in that it was concerned exclusively with plague. Once again Great Britain came under criticism—this time because a serious and persistent epidemic of plague in Bombay had spread to the north-west littoral of India. Austria-Hungary had taken the initiative of proposing the conference, because of the fear that its Moslem subjects returning from the Mecca Pilgrimage might bring with them plague that had been imported by Indian pilgrims. Nineteen other sovereign Powers¹⁶¹ participated in the conference, and there were observers from Bulgaria and Egypt, both of which at that time formed part of the Ottoman Empire. The only distinguished scientist who participated was van Ermengem, the bacteriologist of Ghent. The French delegation included Barrère, Brouardel, and Proust, and another veteran of International Sanitary Conferences, Thorne Thorne, was one of the British delegates. The Italian delegation included for the first time Professor R. Santoliquido, who 11 years

later became the first President of the Permanent Committee of the Office international d'Hygiène publique.

The chief German delegate to the conference stated that it had been intended that Koch should represent his country, but this was not possible as he was in South Africa investigating rinderpest. The only reference made to Pettenkofer during the conference was in the form of a confused version of the localistic doctrine propounded by one of the Spanish medical delegates who said, with reference to plague, that it should not be forgotten that

there are three letters of Pettenkofer: *V*, microbe; *X*, telluric environment, in which meteorology has an unknown influence; *Y*, the organism that is the indispensable factor, and that either does or does not produce the serious disease with which we are concerned; to which I add a fourth letter, *Z*, the disease itself.

That a medical delegate of Spain should have made such a statement indicates that in 1897 Pettenkofer's adherents were not confined to a loyal but shrinking minority in Germany.

In his opening remarks, the chief delegate of Austria-Hungary pointed out that the sanitary convention of 1894 was, after three years, still a "dead letter", as a substantial number of the responsible countries had not yet ratified it. Apart from this, the present conference had to consider whether the dam built against cholera by previous conferences was equally well conceived to resist "the rising tide of Asiatic plague". For France, Barrère declared that the first step required was the ratification by defaulting Powers, especially Turkey, of the 1894 convention. An immediate practical step that was urgently called for, he added, was the banning of departure for the Mecca Pilgrimage by those Powers having Moslem subjects, and France had already banned the Pilgrimage to its Algerian subjects "rigorously and completely". Austria-Hungary believed that it was possible to exercise adequate sanitary control of the small number of its subjects making the Pilgrimage, who then numbered

¹⁶¹ Belgium, Denmark, France, Germany, Great Britain, Greece, Luxembourg, Montenegro, Netherlands, Persia, Portugal, Romania, Russia, Serbia, Spain, Sweden/Norway, Switzerland, Turkey, USA.

only 40–50 per year. Later in the conference, Britain announced that it had imposed a ban on the Mecca Pilgrimage in respect of its Indian subjects for the year 1897. Russia had already taken similar measures in respect of both its Moslem and its Christian subjects. Britain also announced its ratification of the 1894 convention, but with reservations as to the requirement that pilgrims should show that they had adequate means for the return journey, the minimum space allowance on pilgrim ships, and restrictions on maritime communications in the Persian Gulf. Other countries that had not ratified were Portugal, Romania, Sweden/Norway, and Turkey, but the last two subsequently announced their ratifications, Turkey, however, subsequently making important reservations.

On the scientific aspects of plague there was virtual unanimity. Two committees had been established, one technical and the other on ways and means, and van Ermengem as rapporteur of the former was able to declare that it was universally agreed that plague was of microbial origin and that the responsible organism was the bacillus isolated in Hong Kong in 1894 by Yersin. “The susceptibility

of rats, mice, and [other] small rodents is generally recognized.” It was also accepted that outbreaks of human plague were often preceded by epizootics in rats, but there was then no conception of the role of an insect vector in the transmission of the disease. Van Ermengem continued that it had not yet been demonstrated that water could transmit the disease but that the committee thought it prudent to recommend a rigorous surveillance of drinking-water. Thorne Thorne had earlier struck a rather anachronistic note by asserting that “the poison of plague resides particularly in the contaminated soil of dwellings that are unpaved or without floorboards”. The conference agreed on instructions—which were advisory rather than mandatory—for masters of ships, which opened with the following prefatory note:

The transmission of plague appears to take place by the excretions of patients (sputum, dejections), morbid products (suppuration of bubos, of boils, etc.), and consequently by contaminated linen, clothing, and hands.

In 1884, the German cholera commission had had a signal success in British India. Ten years later,

Alexandre Yersin (1863–1943), a disciple of Pasteur and colleague of Emile Roux, was never directly involved in international health activities, but his discovery of the plague bacillus in Hong Kong in 1894 fundamentally influenced the discussions at the tenth International Sanitary Conference, which was entirely devoted to plague. Shibasaburo Kitasato of Japan, who arrived in Hong Kong as head of a mission a few days before Yersin, is widely credited with having been the co-discoverer of the plague bacillus, but his own writings and those of his Japanese contemporaries show that he was mistaken. Writing from Hong Kong to his mother on 24 June 1894, Yersin complained that the Japanese mission had bribed the hospital personnel not to give him facilities for performing autopsies, but added that he had complained to the Governor of the island with satisfactory results. He had, he told his mother, found the plague bacillus: “I always find it; for me there is no doubt.” Signing himself “Your aff. son Dr Yersin”, he asked his mother to wash her hands after reading the letter, but this may have been a pleasantry. Yersin, who spent much of his life in Indochina, founded the medical school of Hanoi and transformed the laboratories of Nha-Trang and Saigon into Pasteur Institutes.





Léon Charles Albert Calmette (1863–1933, seated) was a member of the French delegation at the eleventh and twelfth International Sanitary Conferences held respectively in 1903 and 1911–1912 in Paris. A disciple of Pasteur, he became Director of the Institut Pasteur in Saigon, then in 1894 of that of Lille, and in 1919 Assistant Director of the Institut Pasteur of Paris. Albert Calmette, as he was generally called, made numerous important contributions to medical bacteriology and immunology, as did so many of Pasteur's immediate disciples. While in Saigon he developed antisera for snake venoms and undertook research on ankylostomiasis. Later his interests turned to devising an immunoprophylactic weapon against tuberculosis. Calmette is here shown with Camille Guérin. The names of both Calmette and Guérin are immortalized in the acronym BCG—which stands for “Bacille Calmette-Guérin”. This is an attenuated strain of the bovine tubercle bacillus which is now, after many years of controversy, universally recognised as a vaccine with a high degree of efficacy in protecting against tuberculosis. Robert Koch had discovered the tubercle bacillus in man in 1882, and it was his school in Berlin and that of Pasteur in Paris that between them laid the foundations of medical microbiology.

a Swiss turned French had had a similar success in another part of the British Empire—Hong Kong. But the plague epidemic in Bombay became the scene of what could, in more senses than one, be described as an international rat-race to elucidate the epidemiology of the disease. During the second week of the conference, the German delegation announced that a four-man medical mission had been sent to Bombay headed by Gaffky—Koch being in South Africa. Russia then announced that it had sent a three-man mission, Austria-Hungary that a mission of four physicians had just arrived, and Italy that the first reports had just been received from an Italian physician sent to Bombay. The next

year the British established the Indian Plague Commission, which was some years later to provide conclusive proof of the role of the flea in the transmission of plague.

The conference resulted in a convention dealing solely with plague and signed by all participating countries except Denmark, Sweden/Norway, and the USA. It closed on 19 March, having unanimously expressed the wish that an international committee should be constituted to codify and consolidate the sanitary conventions of 1892, 1893, 1894, and 1897. It also agreed that the text of the last of these conventions should be communicated to the Sanitary Council of Tangiers.

The eleventh conference: Paris, 1903

The eleventh International Sanitary Conference met in Paris from 10 October to 3 December 1903. There were only eight plenary sessions, most of the time being taken up by meetings of a technical committee and subcommittee, a committee on ways and means, and a committee and subcommittee on codification. The last-named of these was to study the consolidation of the four existing international sanitary conventions into a single instrument, while the main task of the committee on ways and means was the elaboration of a proposal—originally made by Adrien Proust at the 1897 conference—for the establishment of a permanent international health

office. Twenty-three sovereign States were represented,¹⁶² and the French delegation included not only the veteran triumvirate Barrère, Brouardel, and Proust, but also Albert Calmette, and Emile Roux. Other delegates who were to occupy the pantheon of medical history were Ion Cantacuzino of Romania, W. C. Gorgas of the USA and, from Germany, Georg Gaffky and Bernard Nocht (the founder and first Director of the Hamburg Institut für Schiffs- und Tropenkrankheiten). One of the

¹⁶² Argentina, Austria-Hungary, Belgium, Brazil, Denmark, France, Germany, Great Britain, Greece, Italy, Luxembourg, Montenegro, Netherlands, Persia, Portugal, Romania, Russia, Serbia, Spain, Sweden/Norway, Switzerland, Turkey, and the USA.

This bust of Ion Cantacuzino (1863–1934) of Romania was presented to WHO by the Romanian Government and now adorns the building that is the seat of the WHO headquarters. Cantacuzino was a pioneer of the introduction of scientific public health measures both at the national and the international levels. He represented his country at the eleventh (1903) and thirteenth (1926) International Sanitary Conferences, and was a member of the permanent committee of the Office international d'Hygiène publique and of the Health Committee of the League of Nations. Before embarking on the study of medicine in Paris he had prepared himself by obtaining from the Sorbonne first a degree in philosophy and then one in natural sciences. Thus equipped, he went in 1891 to work in Metchnikov's laboratory in the Institut Pasteur, Paris, at the same time continuing his medical studies. He graduated M.D. in 1894, and the subject of his thesis—"Researches into the mode of destruction of the cholera vibrio in the organism. Contribution to the study of immunity"—foretold his later interest in public health. In 1901 Cantacuzino returned to Romania as Professor of Experimental Medicine at Bucharest, and later he became Director-General of the Romanian public health service. During World War I he directed campaigns against epidemics of cholera, typhus, and relapsing fever. In 1921 a Romanian law was enacted providing for the foundation of the "Dr I. Cantacuzino Serum and Vaccine Institute", which continues to be an important centre of medical research. In 1928 Cantacuzino founded the *Archives roumaines de Pathologie expérimentale et de Microbiologie*, which quickly obtained a worldwide reputation and still flourishes.



delegates of Turkey, representing Egypt, was Dr (later Sir) Marc Armand Ruffer, who, six years before, had for the first time isolated the El Tor vibrio from five pilgrims with non-choleraic intestinal infections.

The initiative for proposing the conference had been taken by Italy because, as explained by the chief Italian delegate, Rocco Santoliquido, new knowledge of the etiology of pestilential diseases, and especially of plague, had brought with it the need to revise international quarantine regulations. Barrère, who had been elected unanimously to the presidency of the conference, made three main points in his speech of acceptance: the need to codify and consolidate the conventions of 1892, 1893, 1894, and 1897; the modifications to the last of these necessitated by the recognition of the fundamental role of rats in the epidemiology of plague; and the need for a permanent international health office to centralize epidemiological information and keep international quarantine arrangements under review. At the next plenary session Barrère asked delegates, "in conformity with precedents", to keep their deliberations "secret". Such a concept of the confidential nature of the discussions goes far to explain the rarity of the printed proceedings of the conferences.

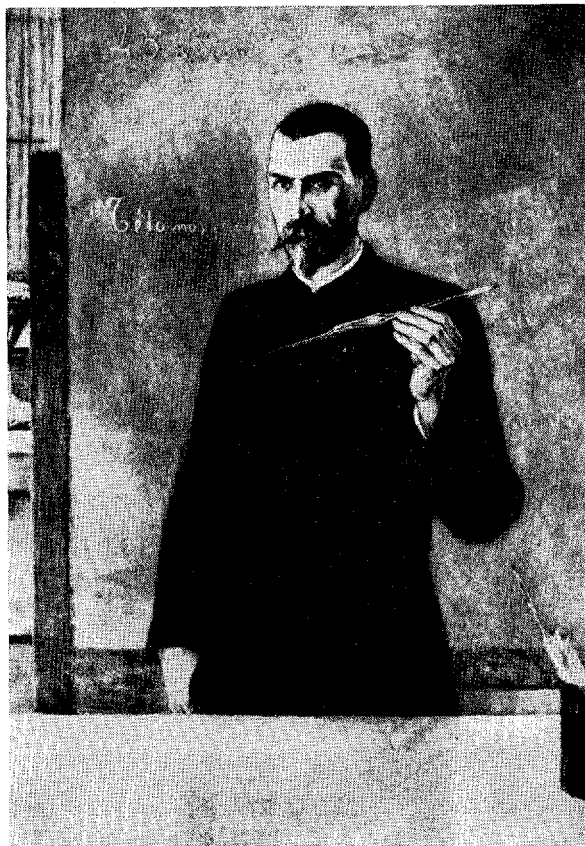
The next speaker, Proust, had every claim to be considered the doyen of international relations in the field of health. He had been a delegate at every International Sanitary Conference since 1874, except for the anomalous conference in Washington in 1881, and was the author of several monographs relating to what he called "the defence of Europe" against exotic diseases. Reviewing the results of the first six conferences, he pointed out that, although they had all failed to achieve an international treaty, they had not been without influence on the sanitary practices of some States and had contributed to the disappearance of "excessive, absurd, and even barbarous" measures. But the seventh conference at Venice in 1892 had been the first to achieve more tangible results. "Thus, it took us 41 years to obtain agreement between the various European Powers on sanitary questions." Among the achievements of the seventh conference had been the organization of sanitary surveillance at Suez and the creation at the Wells of Moses of a hospital, a lazaret, a disinfection centre, and a corps of sanitary guards. It had also reorganized the Sanitary Council of Alexandria. The eighth conference had been concerned with the measures to be taken by governments when there was an outbreak of cholera in a neighbouring State, and the ninth with the sanitary



National Library of Medicine, Bethesda, Md., USA

Adrien Proust (1834–1903) was a member of the French delegation to the fourth, sixth, seventh, eighth, ninth, tenth, and eleventh International Sanitary Conferences, which spanned the period 1874–1903. Already in 1873 he had published a book on international hygiene—*Essai sur l'hygiène internationale*. Ten years later he published a monograph on cholera, but this turned out to be ill-timed, for it preceded Koch's incrimination of the cholera vibrio by only a year. In 1885 he was appointed Professor of Hygiene at Paris. Among his many other publications was *La défense de l'Europe contre le choléra* (1893), the title of which reflects the main theme of the International Sanitary Conferences of the 19th century: the protection of Europe against the importation, especially by sea, of exotic diseases. Proust actively promoted the idea of establishing a permanent international health office but was not to see the realization of his ideal, for while a delegate at the eleventh International Sanitary Conference in 1903 he died a few days before its conclusion. Adrien Proust was the father of the more famous Marcel.

Emile Roux (1853–1933), the eminent French bacteriologist, was a member of the French delegation to the eleventh (1903) and twelfth (1911–1912) International Sanitary Conferences. He was assistant director of the Institut Pasteur under Pierre Emile Duclaux, and on the death of the latter in 1904 became the Institute's third director, a post that he held until his death. Roux is best remembered for his work with Alexandre Yersin on diphtheria toxin, but he also did important work on anthrax, rabies, syphilis, tetanus, and tuberculosis. A distinguished British bacteriologist and historian of his subject said of him: "As an original worker, teacher, and inspirer Roux is regarded as the greatest French exponent of bacteriology after Pasteur." Roux was not directly concerned with the three pestilential diseases that were the subject of the eleventh and twelfth International Sanitary Conferences, but he participated actively, and with great authority, in discussions of scientific questions.



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regulation of the Mecca Pilgrimage and the protective measures to be taken against cholera in the Persian Gulf. These three conferences had all resulted in international sanitary conventions relating to cholera, as had the tenth conference in 1897 in respect of plague. Finally, Proust stressed the need for the establishment of an international sanitary bureau. Surprisingly, he made no reference to the fact that the American States had already combined in the previous year to establish in Washington the International Sanitary Bureau—later to be renamed the Pan American Sanitary Bureau.

The discussions of both the conference and its committees revealed a general realization that there was a need not only for a consolidation of the existing four international sanitary conventions but also that they should reflect the newer knowledge of the etiology of plague and yellow fever (although, in fact, no serious attention was given to the latter disease). It had become clear that the main targets of the control of cholera, plague, and yellow fever were entirely different—human excrement, rats, and

mosquitos respectively—and that a new and unified convention must reflect these differences.

It was the technical subcommittee, with Roux as rapporteur, that had the main responsibility for formulating agreement on scientific questions, and the main subject of its deliberations was the epidemiology of plague. All agreed that plague was transmissible from man to man, that rats played a role in its transmission, and that epidemics of human plague were preceded by epizootics in rats. However, there was no consensus on the role of the flea, although 6 years before in Formosa Masanori Ogata had demonstrated the presence of plague bacilli in the fleas of infected rats and concluded: "Fleas found on plague-infected rats contain virulent plague bacilli, which can convey the poison of plague to man after the death of the rats."¹⁶³ Calmette, and W. P. Ruijsch¹⁶⁴ of the Netherlands, were convinced that fleas were the intermediate hosts of plague, but Gaffky and Roux, while not

¹⁶³ Ogata, M. (1897) *Zbl. Bakt. I. Abt. Orig.*, 21, 769.

¹⁶⁴ Also spelled Ruysch.

excluding this possibility, regarded the evidence in support of it as insufficiently conclusive to enable the conference to reach a firm decision, and this was the position that was adopted. There was unanimous agreement that water played no part in the transmission of plague. On the contrary, all participants recognized the great importance of water in the transmission of cholera, and the theories of Pettenkofer—now dead for two years—were not mentioned. As Barrère had said at the inaugural session: “The prophylaxis of cholera is known. It has been reduced to its simplest terms.”

However, outside the framework of the conference, Pettenkofer's doctrines were far from dead, his two most zealous disciples being his successor to the Chair of Hygiene in Munich, Rudolf Emmerich, and Friedrich Wolter of Hamburg. In the year following the conference, Emmerich testified as an expert witness before a German court of law that neither cholera nor typhoid could be waterborne.¹⁶⁵

While none of the other participants showed the least interest in yellow fever, the presence of Gorgas in the United States delegation made some discussion of it mandatory. In the technical subcommittee, Roux briefly summarized the findings of the American Yellow Fever Commission and then called upon Gorgas to give a fuller exposé, but his

fellow delegate, Geddings, explained that Gorgas had some difficulty in expressing himself in French and would draw up a note on the subject. This he did, and a French translation of the note was read by Ruffer “in the name of the delegation of the United States” at the third session of the technical committee on 31 October. The main point of Gorgas's note was that, as yellow fever was now known to be transmitted from man to man only by the *Aedes aegypti*¹⁶⁶ mosquito, the current international quarantine regulations against it were no longer relevant. He concluded by saying that he hoped that measures against anopheline mosquitos would result in the disappearance of malaria¹⁶⁷—an early intimation of the concept of malaria eradication.

At the previous session of the technical committee Roux had summarized the conclusions of the subcommittee, of which the salient points were that since, thanks to Koch and his pupils, the etiology of cholera had been known for some years, there was

¹⁶⁵ See: Howard-Jones, N. (1973) *Brit. med. J.*, 1, 103.

¹⁶⁶ Then called *Stegomyia fasciata*. Although Carlos Finlay had incriminated this mosquito as the vector of the disease, experimental proof had to await the work of the American Yellow Fever Commission.

¹⁶⁷ The year before, Sir Ronald Ross had been the second recipient of the Nobel Prize for physiology and medicine, for his proof of the role of anopheline mosquitos in the transmission of malaria.



William Crawford Gorgas (1854–1920) was one of the American delegates to the eleventh International Sanitary Conference. In 1901, shortly after the American Army Yellow Fever Commission had provided the final proof of the truth of Carlos Finlay's contentions, Major Gorgas, then nominated chief sanitary officer of Havana, Cuba, cleared the city of yellow fever in a few months by organizing the detection of cases, their isolation under mosquito-proof nets, thus arresting transmission, and the destruction of the insect vector, *Aedes aegypti*. Gorgas then proceeded to clear the Panama isthmus of the disease, so making possible the construction of the Panama Canal. At the Conference, Emile Roux briefly summarized the American work on yellow fever, already recognized as a major triumph of public health, and called upon Gorgas to give a fuller exposé. In his reply, Gorgas emphasized that the newly acquired knowledge of the epidemiology of the disease made obsolete the provisions against it in existing quarantine regulations. He also expressed the hope that the measures that had been so successful against yellow fever would result in the disappearance of malaria. Gorgas fully recognized the debt that the world owed to Carlos Finlay, and in a letter to another distinguished Cuban physician, Dr Juan Guiteras, dated 2 September 1903 he wrote: “I do not know anything in medicine more clear than Dr Finlay's reasoning . . . that the mosquito was the transmitter of yellow fever, and nothing more persevering and plucky than his sticking to the idea, working at it constantly, publishing papers on the subject, from 1881 to 1901.”

no need to modify the protective measures against it embodied in the Dresden convention of ten years before. But, thanks to the newer knowledge of their mode of transmission, this applied neither to plague nor to yellow fever. "The international prophylaxis of each of these [three] scourges should be considered separately."

The outcome of the conference was an international sanitary convention comprising 184 articles, which codified and replaced the conventions of 1892, 1893, 1894, and 1897 and brought international quarantine requirements into line with recent scientific discoveries. This was the first international convention to provide for the destruction of rats on board ship as a protective measure against plague. The convention was concerned exclusively with cholera and plague, except for one short article (182) that paid lip service to yellow fever:

Interested countries are recommended to modify their sanitary regulations in such a way as to bring them in line

with current scientific findings on the mode of transmission of yellow fever, and above all on the role of mosquitos as vehicles of the germs of the disease.

Thus, the eleventh International Sanitary Conference in 53 years had as its essential purpose the protection of Europe against the importation of exotic diseases from the East, and the overwhelming majority of the participants evidently regarded the control of yellow fever as a domestic concern of the Americas.

Article 181 of the convention was of great importance, for it provided that the French Government should, when it judged the moment opportune, propose through diplomatic channels the establishment of an "international health office at Paris". Adrien Proust, who had done more than anyone to promote the foundation of such an office, was not to see his idea realized, for he died only a week before the closure of the conference.

The founding of the Office international d'Hygiène publique: 1907

On 3 December 1907 a "Conférence pour la Création d'un Bureau international d'Hygiène publique" opened in Rome, to agree on the statutes for a permanent international health office, a draft of which had been drawn up by the French Government. This was an international meeting of very precise and limited scope and was not one of the International Sanitary Conferences, although it is sometimes designated as such. The governments of the Americas had already joined together in 1902 to establish in Washington the International Sanitary Bureau—renamed the Pan American Sanitary Bureau in 1923. Twelve countries sent delegations to the Rome conference, which lasted only a week, two of them (the USA and Brazil) being from the Americas.¹⁶⁸ Austria-Hungary, Germany, and the Scandinavian countries were conspicuous by their absence. On the motion of Santoliquido, Barrère—then French Ambassador in Rome—was elected Chairman, and the meeting proceeded immediately to the discussion of the French draft statutes, which were accepted with minor changes, one of which was that the title of the new organization should be Office international d'Hygiène publique—presumably to avoid confusion between it and the International Sanitary Bureau in Washington. The Italian Government had also prepared draft statutes, which provided that the Office should be concerned only with plague, cholera, and yellow fever. It was finally agreed that the principal object of the Office should be to collect and disseminate facts and documents of general public health interest "and especially relating to infectious diseases, notably cholera, plague, and yellow fever". The outcome of the conference was an *Arrangement* by which the participating governments pledged themselves to establish an international health office, and to which were annexed the agreed statutes. The Office was to have its seat in Paris, with a Director, Secretary-General, and staff, and to function under the authority of a committee composed of delegates of member governments. There were six categories of membership, and each government could decide in which category it should be placed. States in the highest category were to contribute 25 units to the

annual budget, in return for which they had 6 votes those in the lowest category having one vote and contributing 3 units. In practice, this voting system was not used. The total annual budget was fixed at 150 000 French francs.

The Committee held its first meeting in Paris on 4–10 November 1908 at the French Ministry of Foreign Affairs, and Santoliquido was elected its first Chairman. Only 9 member countries¹⁶⁹ were represented, although in later years nearly 60 were to adhere to the Rome *Arrangement*. As had been the case with the eleven International Sanitary Conferences that preceded the establishment of the Office, the orientation was heavily European. The main objective of the Office was the protection of Europe against cholera and plague, just as that of the Washington Bureau was the protection of the USA against yellow fever. At the first meeting of the committee of the Office, the main business was the appointment of a Director and a Secretary-General. A motion that only medical candidates should be eligible for the former office was lost, Barrère protesting that the Office represented "a marriage of diplomacy and medicine". Barrère was not entirely disinterested, for he had up his sleeve the nomination of a diplomat, Jacques de Cazotte, who had been the second member of the French delegation at the Rome conference. Some members of the committee were taken by surprise that it should be proposed that the two key posts in the Office should be filled so early, and asked for a postponement to a later session, but Barrère succeeded in obtaining the election not only of de Cazotte as Director but also of another compatriot, Dr H. Pottevin, as Secretary-General. Moreover, the seat of the Office was in Paris, and French was the only working language. It must, however, be acknowledged that France had pioneered both the idea of the International Sanitary Conferences and that of a permanent international health office.

The second meeting of the committee was held on 6–9 April 1909 in the "provisional headquarters"

¹⁶⁸ The others were Belgium, Egypt, France, Great Britain, Italy, Netherlands, Romania, Russia, Spain, and Switzerland.

¹⁶⁹ The absentees were Brazil, Netherlands, and Portugal.

of the Office at 195 Boulevard Saint-Germain, where it was to remain to the end of its days, four decades later. The Chairman announced that an Italian and a French physician had been appointed to the staff, as well as an American engineer who held diplomas from the Institut agronomique of Paris and "one of the universities of the United States". At the third meeting, held from 19 to 23 October 1909, administrative questions loomed large in the discussions, but at the fourth meeting, from 19 to 23 April 1910, the committee began to tackle technical questions.

At the International Sanitary Conference 6 years before there had been unanimity on the modes of transmission of cholera and yellow fever, but it had been agreed that it was still unproven that the rat flea played a role in the transmission of plague. However, by the time that the Office came into being, the careful investigations of the Plague Commission of India had shown that bubonic plague was transmitted from rat to rat and from rat to man solely by the rat flea.¹⁷⁰ For the fourth meeting of the committee of the Office its Secretary-General, Pottevin, had prepared a report on methods for the destruction of rats, the main practical conclusion of which was that such methods should be directed not only against rats but also against their fleas.

For most of the first 50 years of the predominantly European intergovernmental discussions on health matters, cholera had been the only disease to be considered. Towards the end of this period plague became of equal importance. But at its fourth meeting the committee manifested the first signs of a broadening of interests, extending to health problems other than those related to the pestilential diseases that were the subjects of the International Sanitary Convention of 1903, for there were discussions of measures to ensure that diphtheria antitoxin produced in different countries was of equal potency. Here was the first step towards the establishment of international standards for biological products used for prophylactic, therapeutic, and diagnostic purposes, which was to become such an important part of the work of the Health Organisation of the League of Nations and, later, of the World Health Organization. The committee also discussed the unification of "reporting weeks" for health statistical purposes, and agreed that it was desirable that all countries should follow the example of the majority in counting Sunday as the first day of the week. However, at the committee's fifth session, from 18 to 24 October 1910, the discussions were once again dominated by cholera because of an epidemic in Southern Italy. Pottevin had made a visit of investigation to the affected area—Apulia—and presented to the committee a report on the

situation and on the measures taken by the Italian authorities to combat the epidemic. Santoliquido, the Italian Director-General of Health—who had temporarily ceded the chair to Barrère during the discussion of the Italian cholera epidemic—then amplified the information contained in Pottevin's report. He emphasized the need for another International Sanitary Conference not later than the following year, because of the differences in the interpretation by different countries of the provisions of the 1903 convention, and in this he was supported by several other speakers.

Then Calmette, at the request of several delegates, expounded his views on the problem of healthy carriers of the cholera vibrio. These must, he said, be divided into two classes: first, those convalescing from clinical cholera, who were still excreting the vibrio; then those who had inapparent infections and were excreting vibrios without suffering clinically from cholera. The latter were particularly dangerous, as they were ambulant.

At its last but one meeting the committee briefly returned to the subject of biological standardization, and after some discussion adopted the following resolution:

The committee of the *Office internationale d'Hygiène publique*, considering it desirable that sera, vaccines, and microbial products that can be used for the treatment and prevention of contagious diseases should be subject to international agreement, expresses the wish that the governments of participating countries should concern themselves with the study of the factors involved in such agreement. The committee believes that it should, in particular, draw the attention of governments to the question of antidiphtheria serum as one that could at once be the object of an examination that could lead to practical conclusions.¹⁷¹

The Office had now been in existence for nearly two years, and its membership had risen to 22, not all of them being Sovereign States.¹⁷² At the next session of the committee,¹⁷³ which lasted from 8 to 18 March 1911, the Chairman, Santoliquido, announced that the French Government, acting on the recommendation of the committee, had taken steps to convene another International Sanitary Conference and had asked that the Office should prepare for its deliberations by preparing a revised draft of the international sanitary convention of 1903. Because of the importance of the subject and the time that would have to be spent on it, he proposed that it should be the sole item on the agenda. Santoli-

¹⁷⁰ Government of India, Sanitary Commissioner (1908) *The etiology and epidemiology of plague. A summary of the work of the Plague Commission*, Calcutta.

¹⁷¹ Freely translated from the French original.

¹⁷² Algeria, Australia, British India, and Canada were members.

¹⁷³ In the proceedings of its first few meetings, the committee is variously described as *Conseil permanent*, *Comité permanent*, ("Standing Committee"), or *Comité international permanent*.

quido announced further that the powers that had been represented at the 1903 conference but had not yet joined the Office—Austria-Hungary, Denmark, Germany, and Luxembourg—had been invited to send technical delegates to the meeting. All had responded to this invitation (Germany sent Gaffky). Britain and British India did not send delegates, thus demonstrating by no means for the first time a lack of enthusiasm for international sanitary conventions and a traditional preference for playing quarantine matters by ear rather than by the book. There being no opposing voice to the chairman's proposal, the revision of the 1903 convention became the sole agenda item, thus limiting discussion to cholera, plague, and yellow fever.

Two major technical questions concerning cholera occupied much of the committee's time: the significance of the El Tor vibrio, and the importance of the role of the healthy carrier of the classical cholera vibrio. When in 1897 Ruffer¹⁷⁴ carried out a bacteriological examination at the El Tor quarantine station of the bodies of 5 pilgrims who had had no symptoms of cholera and in whom no lesions suggestive of cholera were found, he isolated a vibrio with all the morphological and cultural characteristics by which the classical vibrio was then known, the only difference being that it haemolysed the red blood cells of sheep and goats. In 1905 F. Gotschlich also found what became known as the "El Tor vibrio" in the bodies of 6 of 107 pilgrims who had died of diseases other than cholera.¹⁷⁵

On the first of these questions there were differences of opinion. Gaffky expressed his conviction that the El Tor vibrio was capable of producing clinical cholera, but Ruffer disagreed with him, although conceding that the question was debatable. Ruffer also recalled that Koch had reported from Calcutta in 1884 that the vibrio that he had isolated there was haemolytic, and he raised the question whether Koch might in fact have isolated the El Tor strain instead of the classical vibrio.¹⁷⁶ In further discussion, the difficulties of the bacteriological diagnosis of cholera were emphasized and, on the proposal of the chairman, it was agreed that a special committee—including Ruffer, Calmette, and Gaffky—should be established to advise on this and other technical questions.

There followed a discussion of almost four hours on healthy carriers of the cholera vibrio, Gaffky citing the case of a carrier who had recovered from clinical cholera but who after six months was still under observation because he continued to excrete vibrios. However, he said, the vibrios usually did not persist for more than a few weeks. It was probable, said Gaffky, that the vibrios passed into

the intestines from the biliary passages. In the previous year a pathologist of St. Petersburg, G. S. Kulescha, had maintained that the bile passages played the same role in cholera carriers as they did in carriers of typhoid. In support of this contention he cited the case of a woman who contracted cholera in November 1908, was pronounced free of infection in January 1909 after many stool examinations, and died of other causes in October of the same year. A post-mortem examination revealed that she was harbouring numerous cholera vibrios in the gall bladder. As pointed out by Kulescha, this woman had been a carrier of the vibrio for a whole year and offered "a highly interesting example of the length of time that cholera infection can persist in the human organism".¹⁷⁷

The committee then briefly discussed the derating of ships, H. D. Geddings of the USA urging, as he had done at the previous session of the committee, that this should be done periodically and systematically on all merchant ships. He was strongly supported by Calmette. E. Castilla of Argentina then drew attention to yellow fever: "As you all know, the Paris conference of 1903... remained absolutely dumb on the question of yellow fever. It limited itself to making a recommendation to the countries directly interested that they should concern themselves with adapting their regulations to new scientific ideas." Since then, the American countries had signed an agreement that had proved very efficacious and could very well be incorporated in a revised international sanitary convention. Castilla's intervention was unfruitful, the main outcome of the meeting being a decision that Pottevin should draw up a statement on the bacteriological diagnosis of cholera, which would be circulated to experts in various countries and reconsidered in the light of their comments.

The next session of the committee, which took place from 3 to 10 October 1911, was held only a few weeks before the twelfth International Sanitary Conference. Once again, Britain was absent, although British India was represented, as on previous occasions, by Sir Benjamin Franklin. The main outcome of this meeting was the approval of the final text of the report on the bacteriological diagnosis of cholera, the first draft of which had previously been circulated to outside experts for their comments.

¹⁷⁴ Previously first Director of the British Institute for Preventive Medicine (now the Lister Institute).

¹⁷⁵ The steps in the discovery of the El Tor vibrio are related in the report of a technical committee appointed by the committee of the Office at its session in October 1911. Ruffer, Calmette, and Gaffky were among the members of this technical committee. Credit for the discovery of the El Tor vibrio is usually attributed erroneously to Gotschlich.

¹⁷⁶ Ruffer's recollection was faulty. Koch did not refer to haemolysis in his reports from Calcutta.

¹⁷⁷ Kulescha, G. S. (1910) *Klinisches Jahrbuch*, 24, 137.

The twelfth conference: Paris, 1911–1912

When the twelfth International Sanitary Conference opened in Paris, Pettenkofer had been dead for over 10 years and Koch for over one. But there were still irreconcilable differences between the “epidemiologists”, who adhered to Pettenkofer’s aberrant theories, and those who had, with Koch as their intellectual leader, laid the foundations of systematic bacteriology. The most prominent of the former school were Rudolf Emmerich of Munich, Georg Sticker of Bonn, and Friedrich Wolter of Hamburg. In 1906 Emmerich and Wolter jointly launched a series of monographs that were together to constitute a veritable museum of spurious arguments from doctrinaire assumptions. The first six volumes shared the series title *Jubiläumsschrift zum fünfzigjährigen Gedenken der Begründung der lokalistischen Lehre Max von Pettenkofers*,¹⁷⁸ but after twenty years this was simplified to *Pettenkofer-Gedenkschrift*,¹⁷⁹ the sixteenth and last volume in the series appearing in 1930.¹⁸⁰

Emmerich and Wolter shared authorship for the first volume in the series, in which they proved to their own satisfaction that the Gelsenkirchen typhoid epidemic of 1901 could not have been waterborne.¹⁸¹ The third volume, published in 1910, was an account of almost 800 pages by Emmerich of Pettenkofer’s soil doctrine.¹⁸² Wolter was the sole author of eleven of the remaining thirteen volumes, but he continued his crusade in other publications. By 1944 he was to have found in Pettenkofer’s “soil theory” the explanation not only for cholera and typhoid but also for beri-beri, brucellosis, cerebrospinal meningitis, diphtheria, epidemic encephalitis, influenza, malaria, poliomyelitis, psittacosis, typhus, and yellow fever.¹⁸³

According to Georg Sticker, whose monograph on cholera of almost 600 pages, published in 1912, was treated as a standard work until comparatively recently, notably by Pollitzer,¹⁸⁴ the “ruling excremental-contact-drinking-water hypothesis” had always proved on exact investigation to be inadequate and erroneous. It was based on “suspicions and speculations”, not on real facts and well-

founded proofs. Epidemiology, he maintained, had shown the fallacies generated by “dogmatic, mystical, bacteriology”, and he accorded special credit to Wolter for having demonstrated with “such an impressive plenitude of observations” how hollow were the pretensions of the contagionists.¹⁸⁵

Nevertheless, although Pettenkofer’s “localist” doctrines were far from dead, no echo of them was heard in the discussions of the twelfth International Sanitary Conference, which opened on 7 November 1911 and closed on 17 January 1912, and at which 41 countries were represented, including China and Siam and 16 countries from the Americas. There was no formal relationship between the conference and the Office international d’Hygiène publique, but the discussions of and studies made by the Office during its first three years of existence provided the conference with invaluable background material. Moreover, the staff of the Office attended and participated actively in the deliberations of the delegates, who included the successors of Koch and Pasteur—Gaffky and Roux—as also Agramonte, Calmette, van Ermengem, Th. M. Madsen (Director of the Statens Serum Institut, Copenhagen), and Ruffer. The veteran Camille Barrère, elected once more as President, briefly reviewed the current situation as regards the three diseases under consideration: cholera, plague, and yellow fever. Showing a characteristic European lack of interest in the last of these, he said that he would “leave it to the representatives of the New World” to provide enlightenment on its prophylaxis. As to plague, the

¹⁷⁸ Jubilee Publication Commemorating the Fiftieth Anniversary of the Foundation of Max von Pettenkofer’s Localistic Doctrine.

¹⁷⁹ Pettenkofer Commemoration Publication.

¹⁸⁰ Wolter, F. (1930) *Die Malaria in Russland in ihrer Abhängigkeit von Boden und Klima*, München.

¹⁸¹ Emmerich, R. & Wolter, F. (1906) *Die Entstehungsursachen der Gelsenkirchener Typhusepidemie von 1901*, München.

¹⁸² Emmerich, R. (1910) *Max von Pettenkofers Bodenlehre der Cholera indica*, München.

¹⁸³ *Med. Welt*, 1944, 18, 345.

¹⁸⁴ Pollitzer, R. (1959) *Cholera*, Geneva (World Health Organization: Monograph Series, No. 43).

¹⁸⁵ Sticker, G. (1912) *Abhandlung aus der Seuchengeschichte und Seuchenlehre, Bd. 2. Die Cholera*, Giessen.

experience of the previous eight years had shown that defensive measures against it could not usefully be modified. But, he continued:

It is quite otherwise with cholera; it is with cholera that this conference should appropriately concern itself. In 1903 we knew little or nothing of its incubation period and of the vehicles of its propagation. Today, bacteriologists have provided us with a whole series of positive and controlled confirmations on this important subject. I must recognize that these profoundly modify the ideas upon which international sanitary legislation is based. Five days were fixed as the period of ingestion [sic], and the system of observation of suspect ships and individuals was based on this period. This principle has not survived the test of experience, largely because of carriers of germs. Analysis of the facts shows decisively today that apparently healthy individuals can carry the cholera vibrio for days and even for months and transmit it to their fellows. A healthy person can transmit the disease without being affected himself. This is one of the great discoveries of these last few years. It is rather disconcerting for the authorities responsible for safeguarding the public health.

Thus did Barrère, succinctly but unerringly, indicate to the conference participants what was the most important problem to which they should address themselves. He was followed by Roux, who paid tribute to the "fine discoveries" of the American yellow fever commission, pointed out that the American States had in 1905 signed a convention for the control of the disease, and suggested that similar provisions be incorporated into the new International Sanitary Convention. Such a solution would evidently have spared the conference from having to devote too much time to the predominantly American problem of yellow fever. Turning to plague, Roux complimented the "English commission" on the work "patiently pursued" in India that had fully confirmed the role of the flea in the transmission of plague. But, as Roux pointed out, these findings called for only minor modifications in the provisions of the 1903 convention.

Endorsing, with his great scientific authority, the stand taken by Barrère, Roux declared that the present extension of cholera made it of "pressing interest". Perfection of bacteriological methods had resulted in a realization of the importance of the role of healthy carriers of the vibrio, and it was necessary to take cognizance of the part that they played in the diffusion of the disease. Roux was followed by Santoliquido of Italy, who referred to the "atavistic terror" aroused by cholera and plague and the "terrifying ravages of yesteryear caused by these infections", which explained the public fears and the consequent pressure on health authorities to take the most exaggerated restrictive measures. "Cholera," he added, "certainly consti-

tutes a more serious and more real menace and peril than plague." Nevertheless, the bacteriological control of all potential cholera carriers coming from infected localities was not feasible. The only practical solution was the organization of adequate sanitary services in each country.

The wisdom and vision of these pioneers of international public health—Barrère, Roux, and Santoliquido—were strikingly demonstrated when, as a result of the cholera pandemic that originated in the early 1960s, modern cholera experts rediscovered "the importance and prevalence of the carrier state" and the fact that cholera does not only occur as "an acute, often highly fatal infection, with purging diarrhoea".¹⁸⁶

Disagreeing with Santoliquido, Ricardo Jorge, Director-General of Health of Portugal, insisted on the need for the detection of carriers by bacteriological control. In this view he was supported by Tatushecu of Romania, who stated that he had statistics showing that "there are epidemics in which the number of carriers far exceeds that of clinically diagnosed patients". However, Ruysch of the Netherlands pointed out that, although thousands of passengers from infected localities had been examined at Amsterdam and Rotterdam, only 7 carriers had been found. Such a meagre result did not justify the very considerable expense involved. Later, R. W. Johnstone of Great Britain, Medical Officer of the Local Government Board, intervened to propose that yellow fever should not be considered at all by a "European conference", and that Article 182 of the 1903 convention—which amounted to nothing but a pious recommendation that the American States should go about their own business—should be retained without additions. As more than one-third of the countries represented at this "European conference" were American, this proposal met with scant enthusiasm, and was later withdrawn by its author.

There were only nine plenary sessions of the conference, the bulk of its work being done by a technical committee (rapporteur Roux) with subcommittees on cholera (rapporteur van Ermengem), plague (rapporteur Calmette), and yellow fever (rapporteur Agramonte), a committee of ways and means, and a committee for editing and codification. The relative importance attributed to each of the three diseases under consideration is well illustrated by the number of countries participating in the subcommittees (cholera 32, plague 23, yellow fever 18) and the length of their minutes (165, 52, and 30 printed pages respectively).

¹⁸⁶ Araoz, J. de et al. (1970) *Principles and practice of cholera control*, Geneva, World Health Organization (Publ. Hlth Pap., No. 40).

Presenting the report of the subcommittee on cholera to the technical committee, van Ermengem declared:

The most delicate, the most difficult, and the most serious question inscribed on our agenda was certainly that of the importance of carriers of germs in the propagation of cholera . . . Without being new, because it was already clearly posed in 1893, this question of carriers of cholera vibrios only assumed its present amplitude and acuity since, thanks to a number of extraordinary proofs, the predominance of the role of carriers of bacilli in the endemicity of typhoid fever was recognized.

The subcommittee had agreed on the following definition of cholera carriers:

Carriers of germs are persons convalescing from cholera, or not having presented any symptoms of the disease, who excrete, continuously or intermittently, cholera vibrios in their dejections.

Van Ermengem then turned to the difficult question of the practical results that were to be expected from routine stool examinations in different circumstances. Travellers arriving at land or sea frontiers from suspected localities were rarely carriers. Thus, in the first 5 months of activity of German sanitary posts established at Russian frontiers, only 3 out of 5200 stool examinations had been positive for the vibrio. Similarly, bacteriological control of 7338 passengers and crew of some 30 ships arriving in Rotterdam and Amsterdam from the Baltic had yielded only 3 and 4 carriers respectively. In Naples, of 2000 emigrants departing for America only 12 had been found to be carriers. Conversely, where cholera was epidemic, many more healthy carriers were found. Thus, in St Petersburg, 6% of those who had been in contact with declared cases of cholera were found to be carriers, and in Austria the proportion had risen to as high as 50%.

In the discussions of the subcommittee there was universal recognition of the existence of healthy carriers of the cholera vibrio, the debates hingeing on the extent of the threat to health that they represented and on whether routine bacteriological examination of the stools of large numbers of persons were feasible and worthwhile. Cassim Izzedine Bey of Turkey was the only delegate who questioned whether vibrios that remained inoffensive in the intestines of their carriers could produce cholera in other persons. Richard-August Wawrinsky of Sweden, while not questioning that carriers were potential sources of infection in favourable circumstances, pointed out that in 1909 Swedish ports had received 638 and in 1910 743 ships from ports in Russia, where cholera was rife. There must have been many carriers among the passengers, but nevertheless there had been only

one case of cholera in Sweden in the past few years. This demonstrated, he said, that "in a country where sanitary conditions are good, the danger of the importation of cholera by germ-carriers is minimal". Gaffky raised the question: what was the reasonable maximum length of time during which a carrier could be isolated, that is to say, imprisoned? He cited the case of a carrier in Germany who had excreted vibrios for 250 days and was released from hospital only after 3 stool examinations had proved negative.

Andrea Torella, the Italian delegate to the Sanitary Council of Alexandria, then gave statistics showing the paucity of positive results from the bacteriological control of over 7000 passengers from ships arriving at Alexandria in 1911, but Ruffer, President of the Council, stressed the danger of carriers, as did Daniel Zabolotny of Russia. Ezequiel Castilla of Argentina raised another and very specific point. Recent experience had shown that it sufficed to administer a mild purgative to healthy carriers or to convalescent patients apparently free from their "dangerous guests", to see the latter reappear in the stools. He even knew, he said, of cases in which a purgative administered for demonstration purposes had given rise to serious incidents by provoking true attacks of cholera. Healthy carriers, he maintained, were even more dangerous than declared cases. Johnstone and F. G. Clemow of Britain both supported Castilla's view that the administration of purgatives to presumed carriers could be very dangerous, while A. A. Morrison, the British delegate to the Sanitary Council of Alexandria, pointed out that in the autumn of 1911 the examination of 15 000 stools in Alexandria had resulted in the discovery of only 22 carriers, and concluded: "The game is not worth the candle."

For Ruffer the most important question before the conference was whether or not there should be routine stool examinations of the passengers and crew of short-haul or overcrowded ships coming from infected localities, and Edward Michel of Serbia agreed that the carrier question was "one of the most important, and at the same time one of the most thorny" that the conference had to consider. Clemow had a novel objection to the idea of routine stool examinations. It was well known, he claimed, that one stool might be substituted for another or that, for pecuniary considerations, an innocent stool might be divided into two or more portions, each labelled with the name of a different passenger. Equally practical, but less imaginative, was the objection of Louis Mirman of France: passengers would have to disembark and—"I beg your pardon for these scatological and disagreeable details"—

they would have to be detained for the time necessary for them to make available the product that would be submitted to the bacteriologists. Speaking to the question whether or not cholera carriers could convey the disease at a great distance, Angel Pulido y Fernandez of Spain asked: "What does the word 'distance' mean, when means of transport of persons and goods can attain the vertiginous speed of 112 km per hour [70 mph] or even more?"

The discussions had exhausted every aspect of the carrier problem, and there was almost unanimity as to its importance. There were nevertheless wide differences of opinion as to the feasibility of routine bacteriological control, and the resulting convention contained no specific reference to carriers but left it open to the health authorities of each country to require such bacteriological examinations as they considered to be necessary. In the course of these discussions, Ruffer had made a declaration of fundamental importance, the significance of which was to be lost for many years:

Cholera is entirely multiform, as are typhoid fever, pneumonia, cerebrospinal meningitis, and all infectious diseases without exception, and I am convinced that the so-called classical symptoms occur only exceptionally and that the majority of cases present clinical appearances that have not yet been well studied.

The discussions of the subcommittee on plague revealed few differences of opinion. Zabolotny of Russia gave an interesting account of a mission that he had undertaken, with Haffkine and 11 others, to study the epidemic of the pneumonic form of the disease in Manchuria. There had then been some 10 000 cases, the first of which were seen in hunters of tarbagans. These rodents, a kind of marmot, were hunted for their pelts, of which two million were ex-

ported annually to Europe. Zabolotny and his colleagues had found "pure cultures" of plague bacilli in human cadavers in frozen soil 5-6 months after their interment, while in the putrefied corpses of warmer regions no living bacilli were found. He added that because of the presence of wild rodents near the cemeteries, it had been decided that all pestiferous corpses should be incinerated. Zabolotny had also determined that if Petri dishes containing gelatin culture media were held vertically 0.5-1 m in front of coughing patients with pneumonic plague, numerous colonies of the specific bacilli were obtained. These observations, while of considerable scientific interest, had little relevance to international quarantine, but it was agreed that the dried pelts of tarbagans and human hair harvested from plague victims did not, when exported, constitute a threat to the recipient countries.

The brief discussions of yellow fever centred largely on whether ships, especially those carrying a cargo of bananas, could transport *Aedes aegypti* from the Americas to Europe, and there was a majority view that this was a negligible risk. Henrique de Figueirado Vasconcellos of Brazil pointed out that all that was known of the yellow fever pathogen was that it could pass through a porcelain filter and, in a discussion of whether or not there should continue to be a distinction in the International Sanitary Convention between European and non-European States, made the curious statement that the USA, because of its political importance and strength, was "with justice already considered as a European country".

The final outcome of the conference was a convention superseding those of 1892, 1893, 1894, 1897, and 1903 and containing 160 Articles.

The thirteenth and fourteenth Conferences: Paris, 1926 and 1938

The last session of the permanent committee of the Office international d'Hygiène publique before the First World War was held from 21 April to 3 May 1914. During its short existence, the Office had greatly enlarged the scope of its technical interests. The deratting of ships was still an important topic of discussion, but cholera had faded into the background and yellow fever still aroused little interest. New subjects included brucellosis, leprosy, bovine and human tuberculosis, typhoid, venereal diseases (not forgetting "Ehrlich's remedy"), and water pollution and purification. A further session would normally have been held in the autumn of the same year, but in the meantime the war had broken out.

The first postwar session of the permanent committee of the Office was held in Paris from 3 to 13 June 1919. Opening the session the President, Santoliquido of Italy, referred to the 5 years since the last session as having seemed more like 5 centuries. During that time medicine and hygiene had been entirely subordinated to the war. There was, continued Santoliquido, a need for a complete change of orientation in international health affairs. The idea of erecting barriers against contagion was invalid, and the "quarantine concept" was an obsolete scientific superstition. All efforts should be directed at the elimination of foci of infection at their points of origin, and this could be accomplished only by well-organized health services in all countries. The measures employed must be flexible and in each case adapted to special local circumstances. Active or passive resistance by the public could be countered only by health education. It was necessary to "repair the conscience of the world".

This declaration was greeted with lively applause, and the vision and principles that it embodied seemed to open up the prospect of a much broader and more imaginative conception of the role and responsibilities of the Office. However, important developments that were taking place in a totally different setting rendered any such hopes illusory, for only a few days later the signatories of the Treaty of Versailles subscribed to the Covenant of the League of Nations. This included a provision that Members of the League would "endeavour to

take steps in matters of international concern for the prevention and control of disease" (Article XXIII). Article XXIV laid down that "there shall be placed under the direction of the League all international Bureaux already established by general treaties if the parties to such treaties consent."

On 15 July 1919 the British Minister of Health addressed to the President of the permanent committee of the Office, Dr O. Velghe of Belgium, an invitation to attend an "Informal Conference on International Public Health" in London on 29-30 July to discuss the implications of these Articles of the Covenant. The meeting was attended both by Dr Velghe and Dr Pottevin, Secretary-General of the Office, as well as by representatives of France, the USA, and the League of Red Cross Societies, and resulted in a recommendation that the Office should be placed under the authority of the League of Nations. Velghe reported accordingly at the next meeting, in October 1919, of the permanent committee of the Office, which gave its general assent to this recommendation.

These discussions took place against a background of great urgency, for in war-torn eastern Europe not only was famine taking a terrible toll but there were outbreaks of epidemic diseases on a scale that had not been known in living memory. In Poland there were nearly a quarter of a million cases of typhus in 1919 and in the new Soviet Union over 1 600 000. Moreover, it was estimated that the influenza pandemic of 1918-19 had claimed 15 million lives. It was in such circumstances that the Council of the League of Nations decided on 13 February 1920 that an International Health Conference should be convened in London. The conference met from 13 to 17 April, and only five countries—France, Great Britain, Italy, Japan, and the USA—participated. Belgium and Brazil had also been invited but did not attend. The conference recommended that a permanent international health organization of the League should be established, of which the Office would form a part, and this proposal was approved in its essentials by the first Assembly of the League in December of the same year.



6. Piles of coffins ready for cremation, February 3rd, 1911. Snow lying on the ground.

棺積之葬火備豫 六

From December 1910 to March 1911 there was in Manchuria—the name given by foreigners to northeastern China—an epidemic of pneumonic plague that ultimately cost nearly 50 000 lives. An immediate consequence of this epidemic was the convening in Mukden (Shen-yang) of the “ International Plague Conference ”, in April 1911, at which experts from Austria-Hungary, China, France, Great Britain, Italy, Japan, Mexico, the Netherlands, Russia and the USA participated. Welcoming the delegates, Hsi Liang, the Viceroy of the Emperor of China, conceded that while traditional Chinese medicine had been “ found to be serviceable for many ailments ” it was of no avail against plague. “ We feel that the progress of medical science must go hand in hand with the advancement of learning, and that, if railways, electric light, and other modern inventions are indispensable to the material welfare of this country, we should also make use of the wonderful resources of Western medicine for the benefit of our people. ” At the conference the Chinese Plague Commission presented delegates with a printed album of “ Views of Harbin ”—a town some 200 miles NNE of Mukden. Above is reproduced one of these views, the theme of which is rather far removed from those of photographic souvenirs usually given to foreign visitors. It shows piles of coffins of plague victims waiting to be incinerated. One of the delegates at the conference was D. Zabolotny, Chief of the Russian Commission for Plague Investigation in China, who was also a delegate to the International Sanitary Conference of 1911–1912, at which he described his findings during the Chinese epidemic.

This logical plan foundered on a major political obstacle: the USA was a member of the Office but not of the League of Nations. On 27 April 1921 the President of the permanent committee of the Office wrote to the Secretary-General of the League to announce that the committee declined to be absorbed. Its members, he added, had been

greatly influenced by a telegram . . . according to which the Government of the United States could not consent to any International Organization of which it is a member being combined with the League of Nations.

The Council of the League nevertheless decided on 22 June that it would appoint a Provisional Health Committee which, at its first session from 25 to 29 August, reported to the Council its suggestions for a compromise solution that would take into account “ the fact that the objection of the United States makes it impossible in present circumstances to place the existing Office international d’Hygiene publique in Paris under the direction of the League of Nations ”. Under the proposed arrangement, which was accepted, the Office was to

act in an advisory capacity for certain aspects of the League's health activities.

Thus were to co-exist in Europe, two autonomous international health organizations—respectively in Paris and Geneva—while on the other side of the Atlantic there was a third—the Pan American Sanitary Organization, with the Pan American Sanitary Bureau as its executive organ.

The ideal of a single, worldwide, international health organization was not realized until after the Second World War, but during the inter-war period there was a substantial measure of collaboration between the three organizations. The Office remained in effect an international committee of senior public health administrators served by a small but able permanent secretariat. The Health Organisation of the League, on the other hand, not only disposed of greater material resources but called freely on the services of members of the international community of medical science to advise on a wide range of problems that had not hitherto been the object of serious international endeavours, including malaria, medical education, nutrition, and the international standardization of biological products used in diagnosis, prophylaxis, or treatment. It is possible that the very fact of the coexistence of the two international health organizations in Europe created a certain spirit of rivalry. At all events, the Health Organisation of the League was stimulated to do what had not been done before and may be regarded as the true precursor of the World Health Organization.

One of the main postwar tasks of the Office had been to prepare proposals for a revision of the International Sanitary Convention of 1912 in the light of more recent developments. These proposals were considered at the thirteenth International Sanitary Conference, which was held in Paris from 10 May to 21 June 1926 and attended by delegates of over 50 sovereign states, numerically almost equally divided between Europe and the rest of the world. The conference was opened by the French Minister of Labour, Health, and Social Security. He had been badly briefed, for he expressed the satisfaction of the French Government that for the fourth time Paris should be the seat of this series of conferences. In fact, it was the sixth Paris conference, previous ones having been held there in 1851, 1859, 1894, 1903, and 1911–1912. The Minister was followed by Camille Barrère, who was once again elected President of the conference, and who gave a succinct summary of the results of the previous conferences since that of 1892. Incredibly, at the last plenary session of the conference Barrère, who had been intimately connected with the international sanitary conferences for 35 years, fell into the same

error as his Minister by formally declaring closed the "fourth International Sanitary Conference of Paris".

Among the delegates were some whose names have become part of medical history. Brazil sent Carlos Chagas, who gave his name to Chagas' disease and who was then Director of the Instituto Oswaldo Cruz and a member both of the permanent committee of the Office and of the Health Committee of the League of Nations. Denmark sent Th. Madsen, for many years Director of the Statens Seruminstitut in Copenhagen, Chairman of the League's Health Committee, and a member of the permanent committee of the Office. The French delegation included Albert Calmette—then Assistant Director of the Pasteur Institute—and Léon Bernard, in whose honour the World Health Organization established the Léon Bernard Foundation. Other delegates who were members of both the Health Committee of the League and the permanent committee of the Office were Sir George Buchanan of Great Britain, Ricardo Jorge of Portugal, and Ion Cantacuzino of Romania. Heading the United States delegation was Hugh S. Cumming, who was both Surgeon-General of the United States Public Health Service and Director of the Pan American Sanitary Bureau—a combination of responsibilities that would today seem inconceivable. The 9-man delegation from the USSR was headed by Nicolas Semashko, after whom the well-known institute is named. Representatives of the Office, the Health Section of the League of Nations, and the International Labour Office also participated.

The main task of the conference was to consider what, if any, changes were necessary in the provisions of the 1912 convention relating to plague, cholera, and yellow fever, and whether any other communicable diseases should also be subject to international sanitary regulations. Early in the proceedings Jorge of Portugal struck an optimistic note. The "old triad"—plague and cholera, which had made the Old World tremble, and yellow fever, which had raged in the New—had been robbed of the superstitious terror that they inspired. These pestilences had been tamed. Cholera had become easily manageable; it could be said that yellow fever was almost an extinct disease; only plague struck ports with a certain insistence outside its endemic foci.

Other delegates manifested a more mundane outlook. In particular, Cumming of the USA advanced, in the 76th year of the international sanitary conferences, the revolutionary proposal that French should not be the only language used. English, he said, should be recognized as equal to

French as an "official language", both for debates and for the minutes and also for the text of the convention. All interventions in one language should be immediately interpreted into the other, and there should be official translations of all documents submitted for discussion. However, Cumming was not even assured by the Chairman, as is usually the case when the unexpected happens, that his remarks would be recorded in the minutes, and the only further reference during the remainder of the conference to the use of the English language was a request by another United States delegate, W. W. King, that the protocol of signature should contain an English as well as a French text of a formal declaration that, in signing the convention, the USA would not be implying the recognition of any other signatory "which is not recognized by the United States as the Government of such signatory or adhering Power". This declaration was evidently aimed at the Soviet Union, whose government was not recognized by the United States as the legal one until seven years later. To this request Barrère replied tartly: "It is not possible to give satisfaction to your wish", adding that an English text would be annexed to the minutes. In the event, the English text appeared as a footnote in small print.

The conference appointed three main committees. The first, concerned with scientific questions, established subcommittees on plague (rapporteur Jorge), cholera (rapporteur Cantacuzino), yellow fever (rapporteur Chagas), and epidemiology (rapporteur S. P. James). The task of the subcommittee on epidemiology was to consider whether any communicable diseases other than the classic triad should be included within the provisions of the International Sanitary Convention. The responsibilities of the second main committee were essentially administrative, and especially to review the functions and membership of the Conseil sanitaire, maritime, et quarantenaire d'Egypte (as it was then named) and the arrangements for the sanitary regulation of the Mecca Pilgrimage. The third main committee had the purely editorial function of producing a final text of the convention that was free from ambiguities or inconsistencies and faithfully reflected all decisions reached.

As regards plague, conference participants saw no reason for significant modification of the measures already in force, but reaffirmed that rat control was the essential prophylactic measure, agreeing that in the absence of rats a case of bubonic plague on board had no epidemiological significance. As to cholera, two points were repeatedly stressed: the importance of carriers in the epidemiology of the disease and the great efficacy of anticholera vaccination. The first of these points is fully

in line with the thinking of the 1970s. The second is not, for it is now generally recognized that so far vaccination offers at best very poor protection against the international spread of cholera and that it does not affect the carrier state.

Presenting the report of the subcommittee on cholera, Cantacuzino stated:

Our knowledge on the question of germ-carriers has become more exact; the tendency today is to attribute to them an ever-greater role in the local spread of cholera; observers who have been able to follow on the spot the epidemics of recent wars no longer have any doubt on this question. Moreover, there seems no room for doubt that healthy germ-carriers, or those having had a minimal abortive attack, are able to transport the disease at a distance, this mode of dissemination being necessarily limited by the time, usually rather short, during which the carrier continues to excrete living vibrios.

In the course of the first main committee's discussions, Mitsuzo Tsurumi of Japan had proposed that ships transporting cholera carriers should be treated in the same way as those with declared cases of the disease on board, but Calmette questioned the feasibility of detaining healthy passengers. He was strongly supported by Cantacuzino who, while agreeing that the role of carriers was undeniable, protested that the precautions proposed were "absolutely out of proportion to the danger incurred". The final outcome of extensive debates on the carrier problem was that the conference confirmed the definition of a carrier adopted by the conference of 1911-1912 and incorporated into the final text of the convention two relevant provisions: Article 2 required notification of "the number of germ-carriers in the event that they have been found", while Article 29 contained the painless provision that carriers of vibrios discovered on the arrival of a ship should be "submitted, after they have disembarked, to all the obligations that may be required of the inhabitants of the country of arrival by national laws".

Participants at the conference showed an unbounded faith in the value of vaccination against cholera, the first main committee concluding that "anticholera vaccination is of a certain and well-established efficacy". Calmette stated: "We know today with certainty that anticholera vaccination is easy to apply, harmless, and perfectly efficacious. It is on it that the whole prophylaxis of cholera should be based, and not on the search for carriers." In its report, the subcommittee insisted on "the enormous value of anticholera vaccination" and referred to it as a weapon "whose efficacy is really sovereign", and in a plenary session of the conference Cantacuzino urged that the new convention should provide for systematic vaccination against

cholera. Article 34 of the new convention asserted that "Anticholera vaccination constitutes a method of proved efficacy", and health administrations were urged to apply it as widely as possible. The subcommittee had gone so far as to say that, apart from smallpox and rabies vaccination, there did not exist a more sure or more rapid preventive vaccination than that against cholera.

As to yellow fever, Chagas paid tribute to the researches of Agramonte, Gorgas, Oswaldo Cruz, Juan Guiteras, and also to the Rockefeller Foundation, but added:

It is a certain conclusion of present epidemiology that yellow fever is a disease near to disappearance, and that the measures that must still be included in the convention will soon become useless.

At the 1911-1912 conference, Vasconcellos of Brazil had stated that the yellow fever pathogen was a filter-passing organism, and this had first been demonstrated by the American yellow fever commission of 1900-1901. Nevertheless, the 1926 conference agreed without a dissentient voice that "Yellow fever is propagated by the transmission of the specific germ (*Leptospira icteroides*) by the inter-

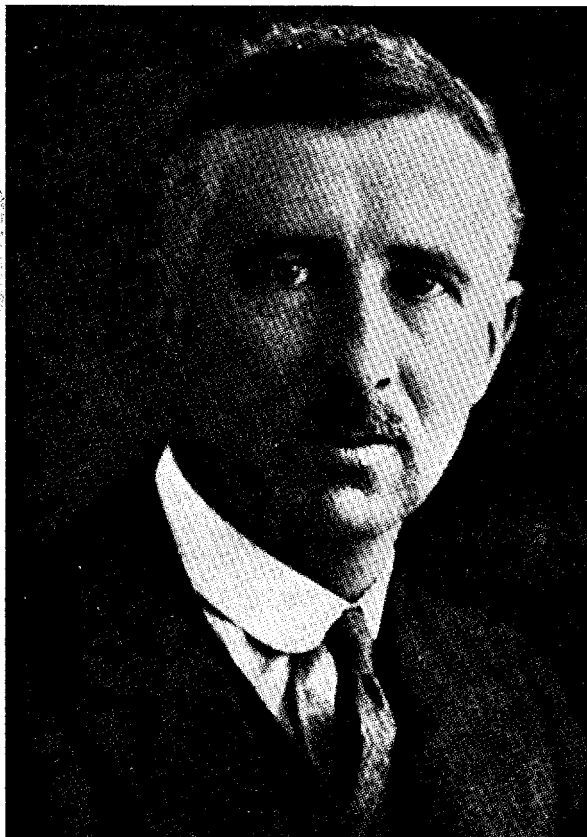
mediary of *Stegomyia calopus* (*Aedes aegypti*).” Thus did the conference confirm at the international level one of the historic errors of medical science, for a few years earlier a Japanese worker, Hideyo Noguchi, had decided in South America that the yellow fever pathogen was a leptospira, doubtless having mistakenly diagnosed as yellow fever what was in fact leptospiral jaundice. Later, investigating yellow fever in West Africa, Noguchi realized his mistake but, as had Lazear of the American commission before him, died of the disease himself, in Accra on 25 May 1928. Among other martyrs to yellow fever research were Adrian Stokes, William Young, Maurice Wakeman, Paul A. Lewis, and Theodore Hayne.

In the fourth subcommittee, that on epidemiology, there was substantial support for the idea that influenza should come within the provisions of the convention, but the impracticability of international quarantine measures against this disease was finally recognized. Carrière of Switzerland advanced a similar argument against a Japanese proposal that smallpox should be made internationally notifiable. This disease, he said,

Hideyo Noguchi (1876-1928), a pupil of Shibasaburo Kitasato, who in turn had been a pupil of Robert Koch, was one of Japan's great bacteriologists and made many important observations in his field. He was one of the first to produce experimental syphilis in animals. Transferring his activities to the USA, he became a member of the Yellow Fever Commission of the International Health Board of the Rockefeller Institute for Medical Research. Noguchi's name is particularly associated with yellow fever, the pathogen of which long eluded highly qualified investigators. In 1897 Giuseppe Sanarelli claimed that it was a "bacillus icteroides", but in 1900 the American Army Yellow Fever Commission rejected this claim, believing an unidentified ultramicroscopic organism to be responsible. In 1919 Noguchi thought that he had discovered the pathogen in Ecuador, and named it *Leptospira icteroides*. This error, which won general acceptance for some years, may be explained by the difficulty in differentiating between yellow fever and leptospirosis on purely clinical grounds and by the fact that the two infections may coexist. As late as 1926, all participants in the thirteenth International Sanitary Conference accepted Noguchi's explanation. At about the same time Noguchi went to make further studies of the disease in West Africa, where he recognized that he had been mistaken and redirected his efforts towards identifying the virus and elaborating a vaccine against it. But on 21 May 1928, still working for the Rockefeller Institute, he died of the disease, the infection having been contracted while he was carrying out research in his laboratory in Accra.



From: Clark, P. F. (1959) Hideyo Noguchi, 1876-1928. *Bull. Hist. Med.*, 33, opp. p. 1. Reproduced by permission of the Johns Hopkins University Press.



Adrian Stokes (1887–1927), born in Lausanne, but of Irish origin, went to West Africa to work on yellow fever under the auspices of the Rockefeller Institute for Medical Research. Participants at the International Sanitary Conferences, most of whom were European, had for years shown a minimal interest in yellow fever, regarding it as primarily an American problem. But the weight of historical evidence is that it originated in West Africa and was imported to the Americas by the slave trade. In the course of his researches, Stokes contracted the disease himself and died of it on 19 September 1927 at the age of 40. A young French physician working on yellow fever in Senegal, René Guillet, died of the disease before his 35th birthday. And an English doctor, William Alexander Young, who attended Hideyo Noguchi in his fatal illness, contracted the disease and died of it on 30 May 1928 at the age of 39. These were not the only victims of research on yellow fever, which probably claimed more lives than any other branch of medical investigation. While the etiology of the disease has been well understood for over 40 years, yellow fever is still a public health problem in Africa and South America.

From *Yellow Fever* by G. K. Strode. Copyright 1951 by the McGraw-Hill Book Company Inc. Used with permission of McGraw-Hill Book Company.

has, in reality, no place in an international convention. It is not a pestilential disease in the proper sense of the term; it is, in effect, a disease that exists everywhere: There is probably not a single country of which it can be said that there are no cases of smallpox . . .

In the event, the convention provided for notification of *first confirmed cases* of cholera, plague, or yellow fever, and of *epidemics* of smallpox and typhus. The question of how many cases constitute an epidemic was conveniently disregarded.

During the discussions, several delegates stressed the need to safeguard the independence of the Office, Barrère in particular insisting that it, and not the Health Section of the League of Nations, should be responsible for administering the International Sanitary Convention. He was strongly supported both by Cumming of the USA and Buchanan of Britain.

For some years Egypt had been unhappy at the continuing existence on its soil of the Conseil sanitaire, maritime, et quarantenaire. In Egypt's view, it was an anomaly that there should coexist an Egyp-

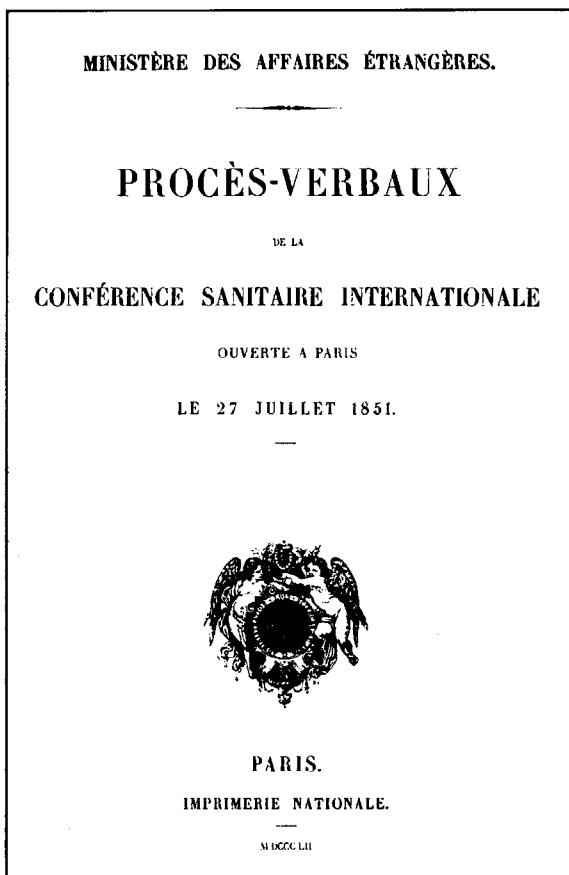
tian public health administration for domestic health matters and an international body responsible for the defence of Egypt against imported epidemic diseases. There was nothing in the responsibilities of the Conseil that could not be adequately assumed by the Egyptian authorities. This contention, however, received no support, and the new International Sanitary Convention contained a special chapter defining the constitution, budgetary arrangements, and responsibilities of the Conseil.

Egypt received satisfaction 12 years later, when, at the fourteenth and last International Sanitary Conference, convened by the French Government at the instigation of Egypt on 28 October 1938, the future of the Conseil was the sole item of the agenda, and it was unanimously agreed that it should be dissolved. Almost 50 countries participated, but this—the last of a series of conferences that had started 88 years before—spanned only 4 days, including a weekend. At the closing session on 31 October, the French Foreign Minister, Georges Bonnet, congratulated Egypt on its “legitimate and enviable” success.

Conclusion

So ended the last of the long series of International Sanitary Conferences that had started some three decades before the beginnings of the age of medical bacteriology. For many years, utter igno-

rance of the causes of the epidemic diseases under discussion provided an insuperable barrier to international agreement. By the time of the seventh conference, in 1892, the nature of cholera was no



More than any other country, France pioneered and promoted the idea of international health cooperation. It initiated the first three International Sanitary Conferences and never ceased to participate actively in persuading other—often reluctant—nations to meet to reach agreement on international measures for the protection of health. Of the fourteen International Sanitary Conferences from 1851 to 1938, seven met in Paris, and the first non-regional international health organization was established in that city in 1908 as the Office international d'Hygiène publique. Here are shown the title-pages of the minutes of the first (1851) and last (1938) International Sanitary Conferences. The former lasted for 6 months, for none of the participants had any real knowledge of the diseases that they were talking about, and its proceedings amounted to 836 pages as compared with 107 for those of the latter, which lasted for 4 days and had only to make a single politico-administrative decision. In their ensemble, the proceedings of these fourteen conferences provide a unique and priceless contemporary reflexion of changing ideas on the nature of epidemic diseases. They show that much of medical history has been grossly oversimplified, and that, for example, Koch's incrimination of the "comma bacillus" as the cholera pathogen was at first widely rejected.

longer disputed at the international level, and at the tenth conference 5 years later the role of small rodents in the spread of plague and the identity of the pathogen were generally recognized. As to yellow fever, the fourteenth and last conference was the first at which the whole story was known.

When Robert Koch discovered the tubercle bacillus he thought that a cure for the disease would soon follow in the form of tuberculin. While this hope was quickly dashed, the discovery of the pathogen did make possible the elaboration of BCG vaccination which, after a stormy history, is now generally recognized as a valuable prophylactic measure. It is otherwise with cholera, for vaccination against this disease enjoys a poor reputation today. Perhaps the chief benefit resulting from the discovery of the cholera vibrio has been in the diagnosis of cases and the detection of carriers, but it has had little effect upon either prevention or treatment. Paradoxically, the country that was most resistant to the germ theory of cholera—Great Britain—was the first to rid itself of epidemics of the disease, and it is universally recognized today that the only real protection against it, as the British sanitarians had consistently maintained, is a pure water supply and the sanitary disposal of human

wastes. Likewise, when the flea was revealed as the missing link in the chain of transmission of bubonic plague from rat to man, prophylactic measures were not affected, for they necessarily continue to be based on the control of rodents, and not of their ectoparasites. The unravelling of the etiology of yellow fever, on the other hand, made possible two powerful weapons against it—direct attack against the insect vector and vaccination. Nevertheless, the hopeful forecast of Carlos Chagas in 1926 is still far from being realized.

The history of the International Sanitary Conferences is largely the history of public health in international perspective. It is more particularly a history of the first gropings towards what is now the World Health Organization, and delegates to the annual meetings of the World Health Assembly are the spiritual descendants of that small band of pioneers who met in Paris on 23 July 1851 to begin six months of discussions. That they met in Paris was no accident, for France was the country that originally, and repeatedly afterwards, took the initiative in promoting international discussions of health questions and in stimulating the establishment of the first non-regional international health organization—the Office international d'Hygiène publique.

Bibliographical notes

Primary sources

For specific scientific developments that took place outside the framework of the International Sanitary Conferences but had a fundamental influence on their discussions, references have been given as footnotes to the text. All such references are to the original publications, which have been consulted directly and not through any secondary sources.

The sources for the discussions at the 14 conferences are their printed proceedings, which together amount to almost 8000 pages. In the proceedings these discussions are summarized in considerable detail, and in some places reproduced verbatim. Except for the Washington conference of 1881, the proceedings were drawn up only in French. The proceedings of the Washington conference were issued bilingually in that language and in English. The titles of the volumes containing the proceedings of the various conferences are of little or no help in locating them bibliographically. These volumes were printed, not as a coherent series, but on an *ad hoc* basis in whichever country each conference was held. In most cases they were entitled minutes (*procès-verbaux*), in some protocols and minutes (*protocoles et procès-verbaux*), and in one protocols (*protocoles*). The volumes were not "published" in the sense of being offered for sale to the public at large, and it is this that explains their extraordinary rarity. For example, the *National Union Catalog of pre-1956 Imprints* shows only two libraries in the USA as possessing the proceedings of the Paris conference of 1851 and none as possessing those of the Paris conference of 1859. The printed catalogue of the British Museum includes only the proceedings of the Vienna 1874 and Paris 1894 conferences and an English translation, published in Calcutta, of the proceedings of the conference of 1866 in Constantinople. In a letter dated 25 July 1974 from the Bibliothèque Nationale, Paris, to the author it was stated that this library possessed the proceedings of 8 of the conferences (3, 4, 6, 7, 9, 11, 12, 14). It is noteworthy that 3 of the missing 6 volumes (1, 2, 13) were printed in Paris by the French government printing office.

For what it is worth, there follows a list of the titles of the various conference proceedings, with some bibliographical notes:

- I. *Procès-verbaux de la Conférence sanitaire internationale ouverte à Paris le 27 juillet 1851*. Paris, Imprimerie nationale, 1852. 836 pages.
Pagination is not continuous, each of the minutes of 48 plenary sessions having separately numbered

pages, as also each of 12 annexes, draft international sanitary regulations, a table of contents, and 3 pages of errata. As is pointed out earlier, the opening date was 23, not 27, July. The conference closed on 19 January 1852.

- II. *Protocoles de la Conférence sanitaire internationale ouverte à Paris le 9 avril 1859*. Paris, Imprimerie impériale, 1859. 277 pages.
Each of the minutes of 37 plenary sessions is paginated separately, as also each of 2 annexes and a table of contents. Three other annexes are paginated continuously with the minutes to which they refer. The conference closed on 30 August 1859.
- III. *Procès-verbaux de la Conférence sanitaire internationale ouverte à Constantinople le 13 février 1866*. Constantinople, Imprimerie centrale, 1866. Tome I, 751 pages; Tome II, 379 pages.
Tome I contains the minutes of 44 plenary sessions, with 8 annexes. All are separately paginated, except that in one case an annex and the related minutes are paginated continuously. Tome II consists of 6 annexes, an "appendice", and a summary of conclusions (*relevé des conclusions*) which was signed by all participants at the last meeting on 26 September 1866. This conference lasted for slightly over 32 weeks and its proceedings total 1130 pages.
- IV. *Procès-verbaux de la Conférence sanitaire internationale ouverte à Vienne le 1^{er} juillet 1874*. Vienne, Imprimerie impériale et royale, 1874. ix+551 pages.
As from this conference, all the proceedings were continuously paginated. This volume contains the minutes of 20 plenary sessions and annexes. The closing meeting was held on 1 August 1874.
- V. *Proceedings of the International Sanitary Conference provided for by joint resolution of the Senate and the House of Representatives in the early part of 1881*. Washington, Government Printing Office, 1881, 449 pages.
The conference opened on 5 January and closed on 1 March 1881, having held 8 plenary sessions. Pages 1-225 contain the minutes of these meetings and some annexes in English, while the French version occupies pages 227-449. There is no title-page in French.

- VI. *Protocoles et procès-verbaux de la Conférence sanitaire internationale inaugurée le 20 mai 1885*. Rome, Imprimerie du Ministère des Affaires étrangères, 1885. xiv+393 pages.
The "protocoles" are the minutes of 4 plenary sessions and the "procès-verbaux" those of 15 meetings of a technical committee. There are a detailed summary (*relevé*) of conclusions and other annexes. The closing meeting was held on 13 June 1885.
- VII. *Protocoles et procès-verbaux de la Conférence sanitaire internationale de Venise inaugurée le 5 janvier 1892*. Rome, Imprimerie nationale de J. Bertero, 1892. xiii+385 pages.
The closing meeting was on 31 January 1892. Minutes of 18 plenary sessions and 7 meetings of a technical committee. Annexes.
- VIII. *Protocoles et procès-verbaux de la Conférence sanitaire de Dresde. 11 mars-15 avril 1893*. Dresde, Imprimerie B. G. Teubner, 1893. xviii+324 pages.
Minutes of 12 plenary sessions and of three committees identified by ordinal numbers and respectively holding 5, 12, and 5 meetings. Annexes.
- IX. *Conférence sanitaire internationale de Paris. 7 février-3 avril 1894. Procès-verbaux*. Paris, Imprimerie nationale, 1894. xii+518 pages.
Minutes of 9 plenary sessions and of 3 committees, again identified only by ordinal numbers and holding respectively 12, 3, and 4 meetings. Annexes.
- X. *Conférence sanitaire internationale de Venise. 16 février-19 mars 1897. Procès-verbaux*. Rome, Forzani et Cie, Imprimerie du Sénat, 1897. xii+518 pages.
Minutes of 15 plenary sessions and of 4 meetings of a technical committee, 11 and 4 of its two subcommittees, and 4 of a committee on ways and means. Annexes.
- XI. *Conférence sanitaire internationale de Paris. 10 octobre-3 décembre 1903. Procès-verbaux*. Paris, Imprimerie nationale, 1904. xv+800 pages.
Minutes of 8 plenary sessions, 8 meetings of a technical committee, 3 of its subcommittee, 8 of a committee on ways and means, 8 of a committee on codification, and 8 of its subcommittee. Annexes.
- XII. *Conférence sanitaire internationale de Paris. 7 novembre 1911-17 janvier 1912. Procès-verbaux*. Paris, Imprimerie nationale, 1912. xxiv+954 pages.
Minutes of 9 plenary sessions, 11 meetings of a technical committee, 4 of a subcommittee on plague, 8 of a subcommittee on cholera, 4 of a subcommittee on yellow fever, 4 of a committee on ways and means, and 7 of an editorial and codification committee (*commission de rédaction et codification*). Annexes.
- XIII. *Conférence sanitaire internationale de Paris. 10 mai-21 juin 1926. Procès-verbaux*. Paris, Imprimerie nationale, 1927. 600 pages.
Minutes of 11 plenary sessions, 15 meetings of a "first committee" (*première commission*), 2 meetings each of subcommittees on plague, cholera and yellow fever, 3 of an epidemiological subcommittee, and 5 of a "second committee" (*deuxième commission*). The number of meetings of the editorial committee (*commission de rédaction*) is not indicated. Annexes.
- XIV. *Conférence sanitaire internationale de Paris. 28-31 octobre 1938. Procès-verbaux*. Paris, Imprimerie nationale, 1939. 107 pages.
Minutes of 3 plenary sessions, 2 meetings of a "first committee", 1 each of a second and third committee, and 1 of an editorial subcommittee. Annexes.

For the activities of the Office international d'Hygiène publique (OIHP) the primary sources are the printed minutes (*procès-verbaux*) of its permanent committee and its *Bulletin mensuel*, which was first published in 1909 and continued without interruption until 1946. The minutes of the inaugural meeting of the permanent committee towards the end of 1908 were not printed. The library of the World Health Organization possesses what appears to be a positive photostat of a typescript of these minutes, on which a former official first of the OIHP and then of WHO, the late M. Georges de Brancion, has indicated in pencil that it is a unique copy. The permanent committee held two sessions per year, that in the autumn being described as "ordinary" and that of the spring as "extraordinary", but there is no apparent reason for this distinction. During the two world wars, no meetings could be held. All OIHP publications were issued only in French.

The origins and evolution of the Health Organisation of the League of Nations are recorded in the League's *Official Journal*, which was published bilingually in English and French, as also were the printed minutes of its Health Committee. Major health activities of the League are reflected in the *Bulletin of the Health Organisation, League of Nations*, which was first published quarterly (under the title *Quarterly Bulletin...*) and then bimonthly. It lasted from 1932 to 1946, and appeared in separate English and French editions. Reports of the Director of the Health Section were appended to the Minutes of the Health Committee, and this committee presented to the Council of the League simplified versions of these as its own reports. The Annual Report of the Secretary-General of the League to the Assembly included a chapter on the work of the Health Section, and Annual Reports of the Health Organisation were published either separately or in its *Bulletin or Chronicle*. The League issued a host of other publications and documents on a wide range of health subjects.

As from 1922, annual and monthly health statistics were published respectively in series E.I. and series R.E. of *Epidemiological Reports*, while from 1926 statistics on the "pestilential diseases" were published in the

Weekly Epidemiological Record, the Eastern Bureau of the Health Organisation publishing similar regional statistics in its *Weekly Fasciculus*. While these statistical publications do not directly throw light on the history of international health organizations, they provide a record of the framework within which such organizations operated for the last half-century.

Secondary sources

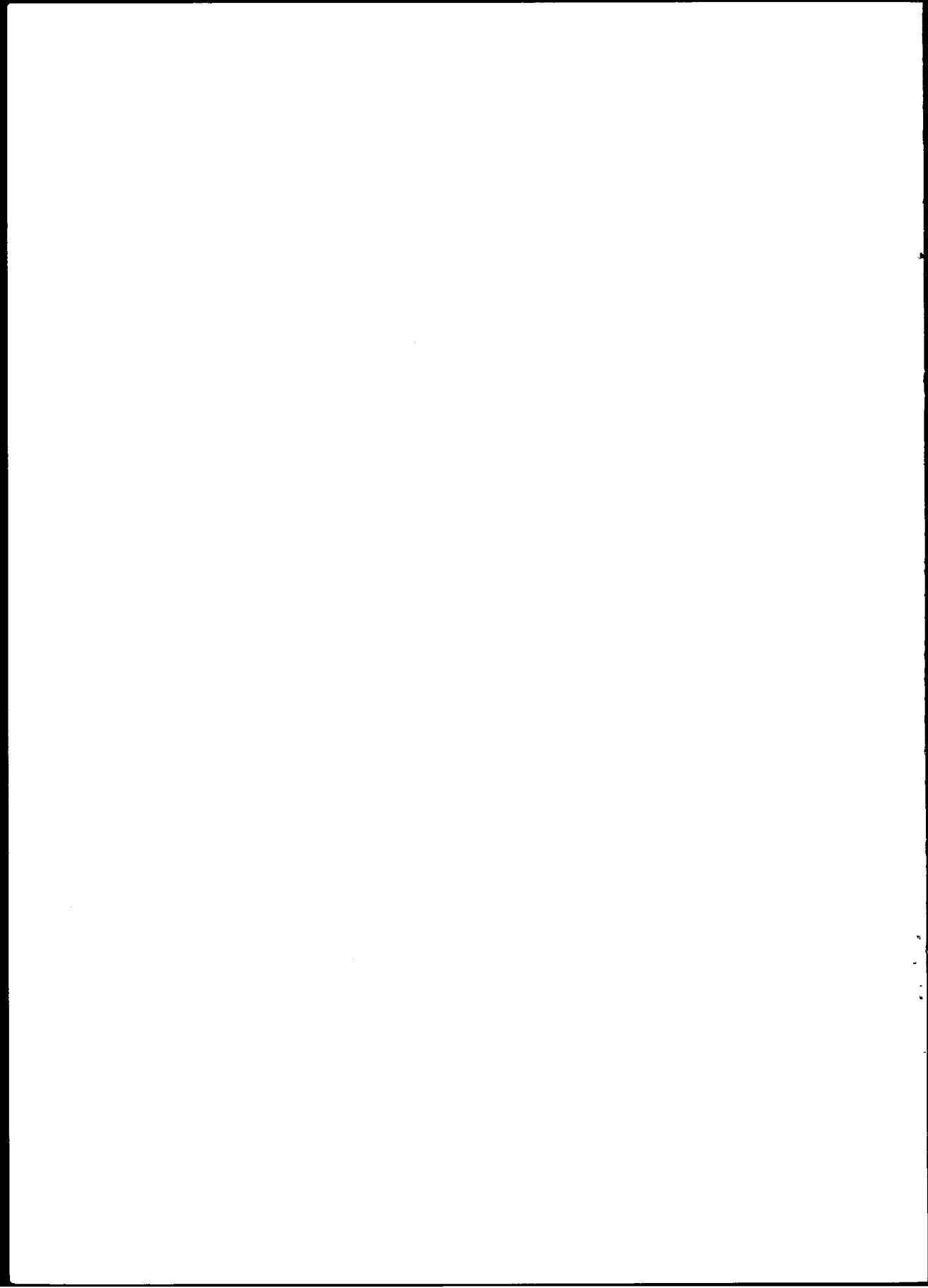
Secondary sources of information on the International Sanitary Conferences are very few. There are brief references to the first 6 of them in two books by Adrien Proust—*Essai sur l'hygiène internationale, ses applications contre la peste, la fièvre jaune et le choléra asiatique* (Paris, 1873) and *La défense de l'Europe contre le choléra* (Paris, 1892). Proust postdates the first conference and antedates the third—in each case by one year. In 1898 J. Lane Notter published a paper on "International sanitary conferences of the Victorian era" (*Trans.epid.Soc. Lond. n.s. 17, 1*), but this is a very superficial account. The October 1943 issue of a commercially sponsored publication, *Ciba Symposia*, was devoted to a short but very useful account of the conferences by Arne Barkhuus, and in 1950 the present author published a brief account of "Origins of international health work" (*Brit. med. J.*, 1950, 1, 1032).

The most systematic account of international health work from its beginnings to modern times is Neville M. Goodman's *International Health Organizations and their Work* (London, 1952), of which a second edition was published in 1971. The present study may be regarded as complementary to Goodman's work, for it is concerned rather with the underlying clash of scientific ideas than with the administrative measures upon which agreement was sometimes reached and sometimes not. The first two

chapters of a WHO publication—*The First Ten Years of the World Health Organization* (Geneva, 1958)—briefly describe international health activities, including the conferences, leading to the establishment of WHO. A most useful, but unfortunately very scarce, work covering most of the active life of the Office international d'Hygiène publique was published in 1933 by its then director, G. Abt, under the title *Vingt-cinq Ans d'Activité de l'Office international d'Hygiène publique*. As to the health activities of the League of Nations, a very useful general description is to be found in the work of Goodman cited above. For those who wish to study these activities in greater depth an invaluable tool is to be found in volume 11 (1945) of the *Bulletin of the Health Organisation, League of Nations*. This consists entirely of a 235-page "Bibliography of the technical work of the Health Organisation of the League of Nations" and lists not only publications but also the numerous mimeographed documents issued on technical subjects.

* * *

In conclusion, it may be said that while the documentation on the earlier international health activities is extensive, much of it is very inaccessible. Not even the world's greatest national libraries—such as the Bibliothèque nationale, Paris, the British Museum Library, London, and the Library of Congress, Washington, have complete sets of the proceedings of the International Sanitary Conferences, and few medical libraries have any of them. It is to be hoped that the availability of modern reprographic methods will encourage medical libraries to provide their users with copies of the texts that are indispensable for the study of the much neglected field of the early history of international health cooperation.



Index*

- ABBATE, PASHA (Egypt), 56
Academy of Medicine, Paris, 10, 47
Academy of Sciences, Paris, 19, 20, 51, 59
ADAMS, M. A., 76
Aedes aegypti, 84
 whether transported to Europe by cargoes of bananas, 92
Afghanistan, 66
AGRAMONTE, A. (USA), 89, 90, 97
ALBER-GLAUSTÄTTEN (Austria), 39, 40
Algeria, 74, 78
ALTSCHUL, J. R., 75
Arrangement of Rome (1907), 86
Association for the Advancement of Medicine by Research, 58
Austria, 10, 12-15, 20, 22, 30, 32, 33, 39, 46
Austria-Hungary, 39, 45, 62, 64, 66, 69, 70, 71, 73, 74, 78, 80, 86, 88, 94
Bacteriology over-valued according to Pettenkofer, but nevertheless the greatest enemy of the "drinking-water theory" (1887), 61
Barcelona Medical Congress, Section of Hygiene, 59
BARRÈRE, C. (France), 63, 64, 69, 70, 71, 78, 81, 82, 84, 86, 89, 90, 95, 96, 98
BARTOLETTI (Turkey), 30, 38, 40
Belgium, 23, 30, 31, 39, 64, 69, 71, 93
BERGMANN, E. VON, 50, 54
Beri-beri, 89
Berlin, 16, 50, 51, 54, 55
Berliner Cholera-Zeitung, 14
BERNARD, C., 20
BERNARD, L. (France), 95
BILLINGS, J. S., 75
Biological standardization, international, 87, 95
BLANE, SIR G., 15
Bombay, 48, 56
BONNET, G., French Foreign Minister (1938), 38
BÖRNER, P., 51
Bosnia-Herzegovina, 71
Brazil, 56, 86, 93, 95
BRÉANT, J.-R., 19
British Medical Association, 52, 58
British Medical Journal, 53, 58, 66, 68
Broad street pump, Pettenkofer's repudiation of Snow's deductions, 61
BROUARDEL, P.-C.-H. (France), 63, 69, 71, 78, 81
BROWN, J. G., 58
Brucellosis, 89, 93
BUCHANAN, SIR G. (Great Britain), 95, 98
BUCHNER, H., 68
BUDD, W., 12, 32
Bulgaria, 78
BURDON-SANDERSON, SIR J., 39, 48, 54, 58, 59
 Koch's incrimination of the cholera vibrio "an unfortunate fiasco", 58, 59
BYKOV (Russia), 32, 33
CABELL, J. L. (USA), 43, 44
Calcutta, 48, 49, 50
CALMETTE, L. C. A. (France), 80, 81, 83, 87-90, 95, 96
Cambridge, University of, 58, 59
CAMERON, C., 52
Canada, 43, 70
CANTACUZINO, I. (Romania), 81, 95, 96
CAPPELLE, VAN (Netherlands), 39
Cardiac catheterization, 10
CARRIÈRE (Switzerland), 97
CASTILLA, E. (Argentina), 88, 91
CATINELLI (Austria), 39
CAZOTTE, J. DE, first Director of the *Office international d'Hygiène publique*, 86
Cerebrospinal meningitis, 89, 92
CHAGAS, C. (Brazil), 95, 96, 97, 100
CHAMBERS, J. S., 49
China, 43, 56, 89, 94
Chinese Plague Commission, 94
Cholera, 9, 12-14, 17-19, 21, 23, 25, 26, 29-31, 36, 37, 40, 43, 46, 49, 52-63, 69-71, 73-77, 82-84, 86-90, 95, 96, 98, 99
 a divine corrective, 15
 air the main vehicle of transmission, 32, 34, 37, 39
 alcohol as an etiological factor, 15, 37, 66
 alleged futility of quarantine measures against, 12-15, 20, 22
 ally of the clergy, 15
 animals, experimental infections, 38, 39, 47-50, 53, 54, 67
 attempts at self-infection, 51, 67, 68
 Berlin conference of 1885, 54
 British refusal to discuss etiology, 55
 British repudiation of quarantine in favour of surveillance, (1883), 56
 British the exporters from India, 74
 carriers, definition (1911-12), 91, 96
 effects of administration of purgatives, 91
 recognition of role, 9, 24, 38, 42, 43, 78, 87, 88, 90-92, 96
 gallbladder as reservoir of the vibrio, 9, 88
 cases, Germany, notification, 38

* The name of a country in parenthesis after a personal name indicates that the person named was an official delegate of that country at one or more International Sanitary Conferences and/or meetings of the Permanent Committee of the *Office international d'Hygiène publique*. In most cases neither the first names of delegates nor their initials were listed. In a few, it has been possible to ascertain them from other sources.

Cholera (*continued*)

- cerebrospinal fluid copious in dehydrated patients, 35, 47
debate between contagionists and non-contagionists, London (1865), 25
declining interest in, by 1914, 93
dehydration, 10, 27, 28, 35
 not regarded by Gaffky as the essential change (1887), 50
dejections contain the moribund agent, 31, 32
"digested" by good digestions, 27
drinking-water, 17, 19, 23, 35-38, 53, 54, 61, 62, 66, 68, 69, 74-76, 78, 84, 89
fear as an etiological factor, 15, 32, 37, 52, 66
first appearance in Europe, 9, 11
"foci of emanations", 27
foreign medical missions in 1831, 10
French and German medical missions to Egypt, 1883
generative principle (unspecified), 31, 37, 38, 39
heat treatment, 16
imported into Europe by sea from Egypt, 1865, 23
Hamburg (1892), 66
incidence in hospital personnel, 26
India, British objections to a proposed international scientific commission, 31
 increase from 1878 to 1892, 74
intravenous infusion, first use, 35
last hidey-hole of the contagionists according to Pettenkofer (1887), 60
main theme of discussion until 1897, 78
"mathematical laws" of Pacini, 27, 28
meteorological influence on, 76
never imported directly from east of Suez to Europe by sea, 57, 63
not communicable, 12, 53, 60
Oranburg the first European town to be invaded, 9
Paris (1832), 18
pathodynamics, 27, 42, 43, 50, 51
quarantine dangerous, 13, 15
recognition of mild or inapparent infections, 9, 92
rehydration therapy, 35, 42, 58
stool examinations for possible carriers, meagre results, 90, 91
stools, black market in healthy specimens, 91
disinfection, 32, 34, 57
vaccination, 58, 59, 66, 69, 96, 97, 100
wide variations in severity, 92
Cholera Commission of the German Empire, 37
Cholera pathogen, *see Vibrio cholerae*
Cholera Regulations, London (1883), 56
Cholera "virus" same as that of typhoid, typhus and smallpox, 20
CLEMOW, F. (Great Britain), 67, 75, 76, 91
CLOT, A. B., his disbelief in contagion, 25, 26
Cold, in treatment of cholera, 16
Commerce, international, hindered by quarantine, 11, 29, 44, 69
Commercial interests and scientific convictions of Britain, concordance of, 57
Conference for creation of an international health bureau, Rome (1907), 86
Conference on International Public Health, informal, London 29-30 July 1919, 93
Congress of Vienna, 1815, map of Europe redrawn, 13
Conseil sanitaire, maritime et quarantenaire, 56, 63, 64, 65, 82, 91, 96
 dissolution (1938), 98
Constantinople, 23, 25, 57
Contagion a mere hypothesis, 14
Cordons sanitaires, 13, 25, 66, 70, 78
CORNISH, W. R., 52
CREIGHTON, C., 33
CRUZ, O., 97
Cuba, 43, 44
CUMMING, H. S. (USA), 95, 96, 98
CUNNINGHAM, J. M. (Great Britain), 42, 49, 52, 53, 61, 71, 74
CUNNINGHAM, D. D., 37, 42
Cyprus, 70

Danube, sanitary regulation of international traffic, 69, 70
Denmark, 23, 30, 39, 64, 70, 80, 88, 95
DICKSON (Great Britain), 33, 74
DIEFFENBACH, J. F., 10
Diphtheria, 89
Diphtheria antitoxin, international standardization, 87
DRASCHE, A., 66, 68
DUNCAN, A., 52
DUPEYRON, P. DE SEGUR, 11
Dysentery, 37

Egypt, 25, 26, 30-33, 39, 40, 46, 47, 49, 51-54, 56, 58, 61, 63-65, 71, 78, 82, 98
EISENLOHR, 67
Emigrants from Europe to the Americas, sanitary control, 73
EMMERICH, R., 54, 67, 68, 75, 84, 88
Encephalitis, epidemic, 89
England, *see* Great Britain
Epidemic, number of cases of cholera constituting, 56
Epidemics, permanent international commission on, proposed (1874), 39, 40
"Epidemic constitution", 12, 53
"Epidemic" diseases regarded by definition as non-communicable, 12
Epidemic influence, its mysterious power, 74
Epidemiological evidence underrated according to Pettenkofer, 61
Epidemiological Society of London, 52
Epidemiology, committee on, 1926, 96
ERISMANN, 76
ERMENGEN, E. VAN (Belgium), 69, 71, 78, 79, 89-91
EULENBERG, 50, 54
Europe as it was in 1851, 13

FARADAY, M. and Father Thames, 21
FARR, W., 17, 27, 28, 29, 43
FAUVEL, S.-A. (France), 29, 30, 32, 40
FAYRER, SIR J. (British India), 52, 53, 54, 55, 59, 60, 74, 75
FERRAN, J., 58, 59, 69
FIGUEIRADO VASCONCELLOS, H. DE (Brazil), 92, 97
FINKLER, D., 54
FINLAY, C. (Spain), 43, 44, 45, 46, 75, 84
FINLAY, C., first public announcement of his theory of yellow fever (1881), 45
FISCHER, 47, 51
FRACASTORIUS "a mere creature of the Pope", 25

- France, 10, 11, 12, 13, 15, 16, 20, 23, 29, 30, 31, 32, 37, 39, 40, 44, 45, 46, 58, 63, 64, 66, 69, 70, 71, 74, 86, 87, 93, 94, 95, 99, 100
 first attempt to convene an international conference, 11
 quarantine, difference of attitudes of Mediterranean and Atlantic ports, 39
 quarantine regulations in 1835, 11
- FRANKLIN, SIR B. (British India), 88
- GAFFKY, G. (Germany) 47, 50, 51, 54, 61, 67, 76, 80, 81, 83, 88, 89, 91
- GAIMARD, P., 10
- GALITZIN, Prince Dimitri Vladimirovich, 51
- Gallbladder the reservoir of cholera vibrios in healthy carriers (1910), 88
- GAMALEJA, N. F., 59, 66, 69
- Gazette médicale de Paris*, 68
- GEDDINGS, H. D. (USA), 84, 88
- GERARDIN, A., 10
- "Gerim", "miasm", "virus", "insect" and other terms used interchangeably by various authors, 25, 31
- German Society for Public Health, 76
- Germany, 37, 39, 63, 64, 68, 69, 74, 80, 86, 88
- GEUNS, VAN (Netherlands), 33
- GIBBES, H., 53, 54
- Gibraltar, 70
- GIETL, F., 32
- GOMEZ (Portugal), 29
- GOODEVE (Great Britain), 31, 32, 33, 74
- GORDON, C. A., 75
- GORGAS, W. C. (USA), 75, 81, 84, 97
- GOTSCHLICH, F., 88
- Great Britain, 12, 13, 14, 20, 22, 29, 30, 31, 32, 33, 36, 39, 41, 43, 45, 46, 52, 53, 54, 55, 56, 57, 61, 62, 63, 65, 66, 69, 70, 71, 73, 74, 78, 88, 90, 93, 94, 95, 100
 belief in general sanitary measures as the only safeguard against epidemic diseases, 52, 66
 cholera, 1848-49, mortality, 29
 expenditure on sanitary improvements, 64
 General Board of Health, 17
 Registrar-General. Twenty-ninth annual report, 27, 28
 Select Committee on Plague (1819), 25
- Greece, 12, 13, 15, 20, 22, 30, 32, 39, 64, 70
- GRIESINGER, W., 31
- GRUBER, M., 75
- GUÉRIN, C., 80
- GUILLET, A., 98
- GUI TERAS, J., 84, 97
- GULL, SIR W., 54
- HAFFKINE, W.-M., 69, 92
- Haiti, 43
- HAMILTON, J. B., 66
- HANSEN, G., 75
- HART, E., 66
- Harveian Medical Society, debate on cholera (1866), 25
- HASSALL, A. H., 17, 33
- HASTERLIK, 68
- HAUSER, P., 68, 69, 75
- Hawai, 43
- HAYNE, T., 97
- Health statistics, unification of "reporting weeks", 87
- Heat treatment of cholera, 16
- Hejaz, first invasion of cholera, 71
- Hejaz, whether cholera endemic, 31
- HENGELMUELLER DE HENGERVÁR (Austria-Hungary), 69
- HERMANN, R., 42
- HIRSCH, A. (Germany), 31, 33, 37, 38, 40, 50, 54
- HÜBSCH (Sweden/Norway), 33
- HUEPPE, F., 75
- Hungary, 39
- HUNTER, SIR W. (Great Britain), 52, 53, 54, 55, 56
- HUXLEY, T. H., 53, 60
- "Hydraulic doctrine" of Pacini, 28
- Incineration of bodies required by Calcutta municipality, 31
- Index-Catalogue of the Library of the Surgeon-General's Office*, 14
- India, 31, 37, 41, 48, 49, 50, 52, 53, 55, 56, 58, 61, 65, 66, 71, 73, 74, 75, 78, 88
 home of cholera, 30, 31, 34, 38, 42
 pilgrimages and the spread of cholera, 30
- Indian Plague Commission, 80, 87, 90
- Influenza, 89, 97
- Influenza pandemic of 1918-1919, 93
- Insanitary conditions predisposing to cholera, 19
- Instituto Oswaldo Cruz
- International bureaux to be under the direction of the League of Nations according to its Covenant, 93
- International commission on epidemics proposed (1874), 39, 40
- International committee on bacteriological nomenclature, 20, 28
- International Sanitary Conference of 1866 "all-contagionist", 30
- International Congress on Hygiene and Demography, 8th, Budapest (1894), 75
- International Health Conference, London, (13-17 April 1920), 93
- International health council proposed for Persia, 40
- International health office proposed, 81, 82, 83, 85
- International health work, scope broadened by *Office internationale d'Hygiène publique*, 87
- International Labour Office, 95
- International Plague Conference, Mukden (1911), 94
- International sanitary agency of notification proposed (1881), 45
- International Sanitary Bureau, Washington, *see also* Pan American Sanitary Bureau, 83, 86
- International sanitary commission at Suez proposed (1866), 31
- International Sanitary Commission, permanent, at Vienna, proposed (1866), 40
- International Sanitary Convention, first draft (1851), 15
 first to come into force (1892), 65, 82
- International Sanitary Convention of 1903 replaces conventions of 1892, 1893, 1894 and 1897, 85
- International Sanitary Regulations, contraventions, 55
 first draft (1851-1852), 15
- Italy, 12, 30, 38, 39, 40, 45, 52, 54, 55, 58, 62, 64, 66, 69, 70, 73, 80, 82, 86, 90, 93, 94
- IVANOVSKY, N., 76
- IZZEDINE, C. (Turkey), 71, 91

- JAENICHEN, 14, 26
 JAMES, S. P. (New Zealand), 96
 Japan, 43, 45, 56, 93, 94, 96
 JENNER, SIR W., 54
 Jidda, 30, 71
 JOHNSTONE, R. W. (Great Britain), 90, 91
 JORGE, R. (Portugal), 90, 95, 96
Journal of the American Medical Association, 68
 Ka'ba, Mecca, 72
Kaiserliches Gesundheitsamt, 66
 KERSCHENSTEINER, VON, 76, 77
 KEUN (Netherlands), 33
 KIERULF (Norway), 39
 KING, W. W. (USA), 96
 KITASATO, S., 75, 76, 79, 97
 KLEIN, E., 53, 54, 58, 61
 KOCH, R. (Germany), 17, 28, 33, 36, 39, 41, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, 58, 60, 61, 62, 63, 65, 66, 67, 68, 69, 71, 74, 75, 76, 77, 80, 84, 88, 89, 97, 100
 KOCH, R., renunciation of his postulates, 49
 scepticism about his incrimination of the comma bacillus as the cholera pathogen (1884), 51, 52
 South Africa, investigation of rinderpest, 78
 superfluity of international efforts in relation to maritime quarantine, 65, 76
Kommabacillus of Koch, 48, 49, 50, 57
 KRAUSE (Prussia), 29
 KULESCHA, G. S., gallbladder as reservoir of cholera vibrias in healthy carriers (1910), 88
 LALLEMAND (France), 32
Lancet, 52, 63, 66, 68
 Land quarantine, 39
 Languages of debates and proceedings, 38, 43, 86, 95, 96, 101
 Latin American countries, 43, 70
 LAVERAN, A., 75
 LAVERAN, A., 75
 Lazarets, 11, 56
 LAZEAR, J., 97
 League of Nations Assembly approves establishment of a permanent international health organization absorbing the *Office international d'Hygiène publique* (1920), 93
 League of Nations, Covenant, 93
 Health Committee, 81
 Health Organisation, 9, 87, 95
 documentation, 102
 League of Red Cross Societies, 93
Legs Bréant, 19
 LENZ (Russia), 29, 32, 33, 39
 Leprosy, 50, 93
 Letters, disinfection of, 11, 70
 LEWIS, P. A., 97
 LEWIS, T. (Great Britain), 42, 55
 Liberia, 43
 Local Government Board, London (1892), 66
 "Localists", 54, 66, 74, 78, 89
 LOEFFLER, F., 75
 Luxembourg, 38, 39, 88
 MACCAs (Greece), 32
 MACLEAN, C., 25, 26
 MACNAMARA, N. C., 75
 MADSEN, TH. M. (Denmark), 89, 95
 Malaria, 12, 23, 53, 60, 84, 89, 95
 Malta, 70
 MANCINI, Italian Foreign Minister, 57
 MARCOVITZ (Romania), 38, 39, 40
 MARKUS, F. C. M., 51
 Marquis of Salisbury, British Prime Minister, 62
 Mecca pilgrimage, 28, 29, 30, 31, 63, 64, 65, 71, 72, 73, 78, 83, 96
 allowance of space on ships, 73, 79
 1897, ban imposed by France, Great Britain, Russia, 78, 79
 cholera, disastrous mortality in 1893, 71
 Moslem subjects of Austria-Hungary, France, Great Britain, Netherlands and Russia, 71, 72
 Medical education, 95
 Medical scientists, individual, direct co-operation in the work of the Health Organisation of the League of Nations, 95
 Medical Society of London, 95, 66
 MÉLIER (France), 13
 MÉNIS, G. M. (Austria), 12, 15
 METCHNIKOV, E., 68, 69, 75, 81
 Mexico, 45, 94
 MICHEL, E. (Serbia), 91
 MILLINGEN (Netherlands), 33
 MIRMAN, L. (France), 91
 MIRZA MALKOM KAHN (Persia), 29, 30, 33
 MONLAU, P. F. (Spain), 13, 29, 32, 38
 MONOD, H. (France), 74
 MORRISON, A. A. (Great Britain), 91
 Moscow, cholera epidemics of 1830 and 1831, 11, 26
 Mouna, 71
 MÜHLIG (Prussia), 29, 32
Münchener medizinische Wochenschrift, 68
 NAPOLEON III, 15
 National Library of Medicine, Bethesda, Md., USA, 7, 9
 Native Passenger Act, India, 31
 Netherlands, 23, 30, 33, 39, 43, 64, 71, 74, 76, 90, 94
 NICATI, W., 58
 NIGHTINGALE, F., 75
 Nižniy Novgorod (Gorkij), 11
 NOCARD, E.-I. E., 46, 47
 NOCHT, B. (Germany), 81
 NOGUCHI, H., 97, 98
 claims that "*Leptospira icteroides*" is the yellow fever pathogen, 1919, 97
 Norway, *see* Sweden/Norway, 39
 Nutrition, 95
Office international d'Hygiène publique, 9, 78, 81, 86-88, 89, 93, 95, 99, 100
 documentation, 102
 to retain responsibility for administering the International Sanitary Convention of 1926, 98
 OGATA, M., 83
 PACINI, F., 17, 20, 27, 28, 33, 34, 35, 37, 38, 42, 43, 46, 47, 48, 51, 52, 64
 Pan American Sanitary Bureau, 9, 95
 Papal States, 12, 13, 20, 22, 23, 30
 PAPON, J. P., 11

- Paris, Austria-Hungary, France and Great Britain meet to amend the 1892 convention, 64
 cholera (1832), 18
 to be seat of the *Office international d'Hygiène publique*, 86
- PASTEUR, L., 46, 47, 49, 59, 66, 89
- PELIKAN (Russia), 32
- PELLARIN, 32
- PERRIER, A. (Great Britain), 14
- Persia, 23, 29, 30, 33, 34, 39, 40, 66, 71, 74
- Persian Gulf, 71, 73, 76, 79, 83
- Persian Gulf, 1894, 98% of shipping British, 74
- PETTENKOFER, M. VON (Germany), 19, 23, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 46, 49, 50, 51, 53, 54, 60, 61, 62, 66, 67, 68, 69, 74, 75, 76, 78, 84, 88
- Pettenkofer's x , y and z , 35, 36, 37, 38, 42, 67, 68, 74, 75, 76, 78
- Pettenkofer-Gedenkschrift*, 89
- PEIFFER, R. F. J., 67
- Pilgrim ships, Arab and Turkish, 31
- Plague, 11, 12, 13, 25, 26, 46, 63, 65, 78, 82, 83, 84, 86, 88, 89, 90, 95, 96, 98, 100
 attempts to disprove contagiousness, 25, 26
 Bombay, epidemic of 1897, 78, 80
 foreign medical missions in 1897, 80
 destruction of rats International Sanitary Convention of 1903, 85
 incineration of corpses, 92, 94
 possible role of drinking-water, 79
 pneumonic, Manchuria 1910-1911, 92, 94
 role of fleas, 79, 83, 84, 87, 90, 100
 role of small rodents, 79, 82, 83
 tarbagans, role of in transmission, 92
 wine as a prophylactic, 11
- Plague bacillus, discovery, 79
 persistence in frozen soil, 92
- Pneumonia, 92
- POLAK (Austria), 32, 33, 39
- POLAK, J., cholera in Warsaw, 76
- Poland, cholera in 1831, 10
 typhus in 1919, 93
- Poliomyelitis, 89
- POLLITZER, R., 49, 89
- POPE PAUL III allegedly bribed Fracastorius to invent the doctrine of contagion, 25
- Porto Rico, 43, 44
- Portugal, 12, 13, 15, 16, 22, 23, 29, 30, 39, 40, 43, 70, 79, 90, 95
- POTTEVIN, H., first Secretary-General of the *Office international d'Hygiène publique*, 86, 87, 88, 93
- PRIOR, J., 54
- Proceedings of the conferences, list, 101-102
 their rarity, 9, 24, 101
- PROUST, A. (France), 15, 37, 38, 56, 63, 69, 71, 73, 78, 81, 82, 83, 85
- Provisional Health Committee of the League of Nations, 1921, 94
- Prussia, 10, 23, 29, 30, 32
- Psittacosis, 89
- PULIDO Y FERNANDEZ, A. (Spain), 92
- Quarantine, diseases originally (1851) regarded as subject to, 13
- Quarantine at Suez, impracticability of disembarking and placing in quarantine all passengers and crew of large ships, 57, 64
- "Quarantine concept" obsolete, 1919, 93
- Quarantine procedures in the 18th century, 11
- Red Sea, 56, 63, 65, 71, 73, 76
- RIETSCH, M., 58
- Rinderpest, Koch's investigation, 78
- Rockefeller Foundation, 97, 98
- Romania, 38, 39, 40, 70, 79, 81, 90, 95
- ROSENBERGER, C. O. R. (Russia), 15
- ROSS, SIR R., 75, 84
- ROUX, E. (France), 46, 47, 49, 75, 81, 83, 84, 89, 90
- ROY, C. S., 58
- Royal Academy of Medicine and Surgery, Barcelona, 59
- Royal College of Physicians, London (1892), 66
- Royal Society of London, 58
- RUFFER, SIR M. A. (Egypt), 82, 84, 88, 89, 91
- Russia, *see also* Soviet Union, 10, 12, 13, 14, 29, 30, 32, 33, 39, 45, 46, 56, 64, 69, 70, 71, 73, 74, 80, 91, 92, 94
 mortality of cholera epidemic of 1892, 67
 mortality of first two cholera invasions, 15, 22
 proposes the 1874 conference, 35
- RUYSCH, W.-P. (Netherlands), 74, 76, 83, 90
- SALEM (Egypt), 32, 33
- SANARELLI, G. claims that "bacillus icteroides" is the yellow fever pathogen, 97
- Sanitary Council of Alexandria, *see Conseil sanitaire, maritime et quarantenaire*
- Sanitary Council of Tangiers, 80
- Sanitary improvements in Bombay, Calcutta, Madras, 31
- SANTOLIVADO, R. (Italy), 78, 82, 86, 87, 90, 93
- Sardinia, Kingdom of, 12, 13, 15, 20, 22, 23
- Saudi Arabia responsible for sanitary control of the Mecca pilgrimage since 1956, 72
- SAWAS (Persia), 33, 34
- Scandinavian countries, 86
- SCOUTETTEN, H., 16
- SEATON (Great Britain), 39, 40
- SEMASHKO, N. (Soviet Union), 95
- SEMMOLA (Italy), 38, 39
- Serbia, 38, 39, 40, 70, 91
- SHAKESPEARE, E. O. (USA), 71
- SHERRINGTON, SIR C. S., 58, 59, 60
- Ships traversing Suez Canal "clean", "suspect" or "infected" with cholera, 64
- Siam, 89
- SILVA MARTINS, J. L. DA, 75
- SIMON, SIR J., 17, 36, 37
- Smallpox, included for the first time in the International Sanitary Convention of 1926, 98
 Japanese proposal that it should be internationally notifiable, 97
 possible application of Pacini's "mathematical laws" to prognosis, 27
 universal, therefore not considered an international problem, 1851, 12
- SNOW, J., 12, 17, 19, 20, 21, 23, 27, 32, 33, 34, 37, 43, 61, 62, 69
- Snow's explanation a "peculiar doctrine", 17

- Société de biologie, Paris, 47
 Soil theory of Pettenkofer, 23, 24, 32, 35, 36, 37, 38, 40, 42, 46, 50, 54, 61, 66, 68, 75, 76, 89
 Soviet Union, 95
 non-recognition by the USA in 1926, 96
 typhus in 1919, 93
 Spain, 12, 13, 14, 15, 20, 22, 29, 30, 31, 32, 38, 40, 43, 45, 58, 63, 64, 70, 78, 92
 Statens Seruminstitut, Copenhagen, 95
 Steam navigation in the Red Sea, 30, 31
 STENERSEN (Sweden/Norway), 33
 Sterilizers in cholera control, 63, 67
 STERNBEG, G. M. (USA), 56
 STICKER, G., 89
 STOKES, A., 97, 98
 STRAUS, I., 46, 58
 STUART (Great Britain), 29
 Suez, 5-day quarantine would make use of canal uneconomic, 57
 Suez, sanitary control at, 56, 82
 Suez Canal, 56, 63, 64, 65, 66
 opening in 1869, 41
 SUTHERLAND, J. (Great Britain), 12
 Sweden, 39, 91
 see also Sweden/Norway
 Sweden/Norway, 23, 30, 45, 64, 70, 73, 79, 80
 Switzerland, 38, 39
 Syphilis, experimental, in animals, 97
- TARDIEU, A., 11
 TATUSHECU (Romania), 90
 Teheran, Sanitary Council of, 40, 74
 Temporary medical council, Moscow, 1830, 51
 THIERSCH, C., 38, 39, 48, 59
 THORNE THORNE, R. (Great Britain), 53, 55, 56, 69, 71, 78, 79
 THULLIER, L., 46, 47
 Tonkin, 74
 TORELLA, A. (Italy), 91
 Transport, vertiginous speed of in 1912, 92
 Transmutability of epidemic diseases, 12, 37, 53, 60
 Treaty of Versailles, 93
 TREILLE, G., 76
 TRESKOW, 47
 TREVISAN, V., 51
 Troopships, British, passage through Suez Canal, 64
 TSURUMI, M. (Japan), 96
 Tuberculosis, 93
 Turkey, 12, 13, 15, 20, 29, 30, 38, 39, 40, 46, 56, 64, 70, 73, 78, 79, 82, 91
 Tuscany, 12, 13, 15, 23
 Two Sicilies, Kingdom of, 12, 13, 20, 23
 Typhoid, 23, 37, 50, 78, 84, 91, 92, 93
 Typhoid epidemic in Gelsenkirchen (1901), 89
 Typhus, 12, 89, 93, 98
- United States of America, 23, 43, 44, 45, 46, 52, 56, 70, 71, 73, 80, 84, 86, 93, 94
 1894, abortive proposal for International Sanitary Conference on importation of cholera to the USA by European immigrants (1894), 73
 Congress, resolution of 1880 authorizing international sanitary conference, 43
 first participation in an International Sanitary Conference (1881), 43
 vetos absorption of the *Office international d'Hygiène publique* by the League of Nations, 94
 Yellow Fever Commission of Army, 44, 84, 90, 97
 University of Cambridge, 58, 59
- VELGHE, O., President of the permanent committee of the *Office international d'Hygiène publique*, 93
 VELPEAU, A. A. L.-P., 20
 Venereal diseases, 93
Vibrio cholerae, 17, 24, 27, 28, 33, 35, 36, 37, 42, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 57, 58, 60, 61, 63, 64, 66, 68, 69, 76, 87, 96, 100
Vibrio cholerae, local action on the intestinal mucosa stressed by Pacini (1879), 42
Vibrio El Tor, 82, 88
Vibrio El Tor, whether or not could produce clinical cholera, 88
 Vinegar as a disinfectant, 11
 VIRCHOW, R., 35, 50, 54
 Voting procedures, 12, 23, 33, 38, 56, 71, 86
- WAKEMAN, M., 97
 Water pollution and purification, 93
 Water supplies in London in 1854, 17
 WATSON CHEYNE, W., 58
 WAWRINSKY, R.-A. (Sweden), 91
 Wells of Moses, 63, 82
 WENDT, E. C., 58
 Wine as a prophylactic, 11
 WHYTE, D., 25, 26
 WOLTER, F., 89
 World Health Assembly, 24
 World Health Organization, 7, 9, 16, 29, 43, 81, 87, 95, 100, 102
- Yellow fever, 11, 12, 13, 25, 37, 43, 45, 46, 56, 63, 65, 78, 83, 84, 86, 87, 88, 89, 90, 95, 96, 97, 98, 100
 cargoes of bananas a risk, 92
 deaths of medical investigators, 97, 98
 lack of interest of European delegates, 84, 85, 88, 89, 90, 93
 scientific sanitary commission proposed, 45
 Yellow fever commission, US army, 44, 84, 90, 97
 Yellow fever pathogen, a filter-passing organism, 92, 97
 claimed by Noguchi to be "*Leptospira icteroides*" (1919), 97
 claimed by Sanarelli to be "*bacillus icteroides*" (1897), 97
 YERSIN, A., 33, 76, 79, 83
 YOUNG, W. A., 97, 98
- ZABOLOTNY, D. (Russia), 91, 92, 94
Zeitschrift für Biologie, 32, 35