CONTRIBUTION TO THE HISTORY OF MEDICINE IN BRAZIL

Reports of

Dr. Adolfo Lutz

as Director of the Bacteriological Institute of S. Paulo

CHOLERA

(1893-1895)

INTRODUCTION

The Bacteriological Institute of the State of São Paulo had hardly been organized when it was called upon to cope with a grave problem. Asiatic cholera broke out on August 13, 1893, at the Hostel for Immigrants, on the outskirts of the city and the Bacteriological Institute was called upon to diagnose it.

Lutz promptly and successfully applied the technique worked out abroad, with a modification or two of his own,. Bacteriological diagnosis of these cases was completed within the day.

This was important because the fact that so dread a disease as cholera should have come within their own sphere of activity was both novel and unwelcome to several prominent members of the medical profession. Rather than acknowledge its presence, they preferred to claim that there must be an error of diagnosis and that ordinary cases of diarrhoea were being labelled as cholera at the Bacteriological Institute. The truth was exactly the reverse. Although light cases of Asiatic cholera are known, those seen by the Public Health authorities of São Paulo were not light but severe, with a high percentage of mortality and clear connections with an epidemic sequence of other cases.

The laboratory evidence, exhaustive in itself, was controlled and corroborated by clinical observation and post-mortems, neither of which were neglected by Lutz. The Institute was kept open to all physicians who wished to check the work done there. The opponents, however, were not eager to argue along bacteriological lines.

While they cavilled over the hypothesis of diarrhoea, Lutz, who was sure of his diagnosis, and had carefully observed the cholera vibrio isolated by him, went on to differentiate it from the germs isolated from cases of
food-poisoning with somewhat similar symptoms. One of these occasioned a false alarm of a very dramatic nature, on Christmas Eve of 1894 at the Immigrants' Hostel. On that day, two thousand, out of the five thousand inmates, fell ill simultaneously with vomiting and diarrhoea. All but one recovered. The one fatal case was subjected to post-mortem examination by Lutz and showed a condition rather different to cholera, without exsiccation of the tissues and in agreement with the bacteriological findings. These are discussed in the correspondence between Lutz and Prof. Dunbar, Director of the Institute of Hygiene of Hamburg, whom he invoked to confirm his diagnosis, since he knew that outside authority was the only form of proof likely to carry conviction to those who opposed him.

The first epidemic was small and short-lived, but in the summer of 1894-1895 a second, and somewhat more extensive, epidemic followed it. Several regions of the state were affected, especially a series of towns along the banks of the Parahyba river. Among Lutz' personal reminiscences of cholera, was that of a small place on a tributary of the Parahyba, where the riverside population was wont to rid itself of the mattresses and bedding of cholera patients by dumping them into the stream.

The two epidemics and the problems they presented are treated at length in Lutz' reports for 1893 and 1894 to February of 1895. After that, no further epidemics of asiatic cholera are mentioned in his reports.

Nevertheless, vigilance was not relaxed. The yearly reports discuss cases of diarrhoea, choleraform enteritis and cholera nostras and their seasonal prevalence, with a marked increase during spells of hot weather.

Excerpts from these reports and the correspondence with Dunbar are given below in English. The full translation of the letters and the unabridged Portuguese text of the reports precede this summary.

CHOLERA

EXCERPTS FROM THE REPORTS OF DR. ADOLPHO LUTZ

1893: SPECIAL REPORT ON CHOLERA

"On August 13th, liquid stools from the Immigrants' Hostel were sent to the Bacteriological Institute. Cholera was suspected, and a bacteriological test was asked for. Until then no cases had been seen but the Director had followed the work done abroad, including that on recent epidemics, very carefully in the literature. Cultures were immediately made in a liquid medium
composed of Witte's peptone 1 grm., sodium chloride 0.5 to 1 gram., and water 100 grms. After neutralising and sterilising, this was inoculated either with flakes of mucus, as advised by KOCH, or with a few drops from the surface of the stools, where the vibrios flock for oxygen. The platinum in use for inoculations was modified by me so as to provide it with a spiral tip. In this medium cholera bacilli multiply rapidly, so that already after from 5 to 8 hours incubation at blood temperature, the bacilli were found in large numbers on the surface. Other intestinal bacteria develop more slowly. By sowing out in fresh tubes almost pure cultures were obtained either by successive dilutions or in solid media on Petri dishes, at the end of another 5 to 8 hours. In some cases they had to be resown three or four times.

The results of this technique proved so satisfactory, even in cases which seemed doubtful on direct examination, that it was systematically adopted. It has the added advantage of making the cholera-red test easy to apply and clear. This consists in adding a few drops of pure hydrochloric or sulphuric acid to the cultures if they are liquid or to a suspension in water of those made on solid media. If the cultures are fairly pure, after 5 hours' incubation a rosy tinge develops and deepens gradually. This is due to the simultaneous presence of indol and small quantities of nitrates. The characteristic smell of indol pervades the cultures and after a little practice it aids diagnosis.

Microscopic examinations were made by drying the flakes of mucus or drops from the surface of stools on slides or cover-glasses and staining them with Ziehl's fuchsine solution. The comma bacilli stain a vivid red. Immersion lens at 1000 diameters was used.

By these methods and the obtention of pure cultures I was able, in about 10 hours time, to inform the Public Health Service, with an almost absolute degree of certainty that the disease was indeed cholera. This diagnosis was confirmed by comparison with the descriptions in the literature and with a culture sent from the Institut Pasteur in Paris which we had in the laboratory and which was labelled "Cholera de Calcutta". It was probably descended from one of Koch's original cultures. As it was very exhausted, it had to be resown and it developed slowly, but after a time it furnished quite typical comma bacilli, identical with those found in the stools.

Identification was based on comparison of the following characters:

1) The size and shape of cultures of the same age, in Petri dishes with gelatine or agar and in tubes of gelose or gelatine, sown by stabbing inoculation or streak.

2) The size and form of the bacilli examined under the microscope, both living and mounted and stained.
3) The appearance and chemical reaction of the cultures in peptone solutions prepared according to Koch's method.

4) The odour of the cultures on liquid and solid media.

Living vibrios from the cultures were also observed, at blood-temperature. They showed active movement and gathered at the edges or around bubbles of air. Long cilia were seen, at one or both ends, in preparations made by Loeffler's method, which yielded some good results. Sometimes there were four cilia but more often one only at one end. The bacillus from São Paulo evidently belongs to the first variety of the cholera vibrio described by Koch. Comparison with Deneke’s bacillus showed the known differences and inoculation in one monkey and two pigeons differentiated if from that of Metchnikoff.

In the next two months a number of stools were examined. All those with cholera characteristics, that is those composed of a more or less cloudy, serous, alvine liquid and a whitish deposit of mucous flakes, without trace of biliary pigments, showed vibrios. Twice they were so abundant as to seem like pure cultures.

In cultures from such stools the cholera bacillus was always found easily, except in one case, in which the cultures remained sterile, a fact which was probably due to the addition of some antiseptic.

Among the stools sent us from different parts of the city there were a few from cases of plain diarrhoea, but these contained biliary pigments and no vibrios were found in them.

I mention this as, at the time, a good deal of opposition arose and attempts were made to descredit the Institute by saying that cholera bacilli were found here even in the simplest cases of diarrhoea. It is a well-known fact that there are extremely light cases of cholera, characterized only by diarrhoea, and that there may also be a premonitory diarrhoea; in both these instances cholera vibrios are present in the stools, sometimes in large proportions. During a cholera epidemic it is a dangerous practice to disregard cases of diarrhoea in which comma bacilli are found. It is precisely in such cases that bacteriological examination is most useful. There must have been some in São Paulo, though, I myself unfortunately, saw none of them.

Towards the end of the epidemic, cholera vibrios were isolated from one stool sent from Caiéiras, which though it was liquid contained biliary pigment. It was not taken at the onset of disease and, the week before, three other members of the same family had died, after from one to three days' illness. Their deaths had been certified as due to copper-poisoning but the symptoms were the same as those observed in some cases of cholera from the suburbs of São Paulo.
At this Institute all work is done conscientiously. Physicians from outside are often present but unfortunately it is just those who deny the existence of cholera who are unwilling to accept our invitations. They prefer to rely on their professional standing alone. With all due modesty, I cannot accept their superior wisdom on the subject and still less concede them the privilege of judging a question of epidemiology without observing any cases.

Vomit was examined a few times and was found positive in a female patient from the Immigrants' Hostel. As a rule, the alvine stools were preferred, as they contained less foreign matter.

Most stools are sent to the Institute without information as to the circumstances and the severity of the case and it is only after reporting on them that we ask for such details. After all, you cannot expect a Bacteriological Institute, which receives a small quantity of stools, often inappropriately gathered, or kept for a long time, to relieve practitioners of all trouble of observing their patients or to exonerate them from all responsibility if they help to spread the epidemic. This said, I may state, with some satisfaction, that whenever I was able to compare them, clinical observations always agreed with the results of bacteriological examinations, that is:

I. The cases in which the cholera vibrio was found proved by their severity, high degree of mortality, tendency to form new foci, or connection with former cases, that they were cholera.

II. Those with choleriform symptoms, but from which cholera bacilli were absent, recovered promptly and were not followed by other cases in the same place. They were probably cholera nostras, most improperly called cholerine. I would like see this name abolished, or at least limited to light cases of Asiatic cholera.

Seven post-mortems were made on fatal cases occurring during the epidemic and in all of them the pathological findings agreed with the results of the bacteriological examinations. One was a simple and somewhat drawn-out case of enteritis. Five showed the classic lesions of cholera. Coma bacilli were found in all five, though only once predominating to the extent of an apparently pure culture. Cultures were easily obtained from the others. The seventh case (a coloured woman of about 45), showed the lesions described for the period of reaction; her stools were not typical cholera stools, being consistent and bilious. Direct microscopical preparations did not show the specific vibrio but it developed in the cultures." (1)

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**NOTE**: The Portuguese text gives a list of cases, summaries of post-mortems and the characteristics of the comma bacillus, which was little known in this country, not having been observed previously.
REPORT FOR 1894 AND JANUARY AND FEBRUARY OF 1895: "CHOLERA"

"Towards the end of 1894, Cholera again appeared in the State of São Paulo, without proof of re-importation from Europe. It began almost simultaneously in São Simão and at Cachoeira, and shortly afterwards in the capital of the State. At São Simão it soon died down, but it continued to spread along the valley of the Parahyba river and in the city of São Paulo. A few other foci occurred during the months of November and December 1894 and January 1895.

Bacteriological, pathological and clinical observations and the course of the epidemic leave no room for doubt as to the nature of the disease. All the protests against the existence of cholera are so devoid of proof or good reasons that they cannot be taken into account.

Bacteriological diagnosis was often asked for during this epidemic, both as to first cases occurring in new localities and so as to determine the cause of death or the nature of illness. I visited Cachoeira, Cruzeiro, Queluz and Rezende, on the Parahyba river, made post-mortems and collected material for bacteriological and microscopical examination. Pure cultures of the cholera vibrio were obtained.

Out of the 19 post-mortems made in São Paulo city, 14 were cases of cholera in the acute or typhoid period. There were also two of chronic enteritis; one case of fish poisoning; one perforation of a typhoid ulcer and a case of gangrene of the ileum. In 36 stools, of persons resident and taken ill in the capital, there were 23 cases of cholera in the acute or typhoid period; 2 stools had been sterilized but showed typical bacilli; in 4 they were so abundant as to seem pure cultures. There were also eight cases of non-infectious gastro-enteritis; two cases apparently of cholera nostras, which were cured; one death with uncertain diagnosis and one from pulmonary and intestinal tuberculosis. In one post-mortem there were no traces of intestinal disease to be seen.

Stools from São Simão, Taubaté, São Carlos, Barueri and Guaratinguetá were also examined. Those from the two last places were positive. The others were negative but the stools had probably been kept long or disinfectants added.

It should be remembered that to obtain accurate results in bacteriological examination only small samples are needed, but they must not contain chemicals, which prevent the vegetation of the comma bacillus, nor should examination be delayed unduly.

Bacteriological examination should not fail if the observer is careful and skilful and uses the processes generally adopted. We never failed to get positive results in genuine cases, in which we had gathered the specimens
ourselves, even if the post-mortems had been delayed or if the patients were in the typhoid period. In the latter, the contents of the gall-bladder always contained the vibrio, sometimes in pure culture. It should always be examined in the other cases also. Twice the contents were serous and quite devoid of pigment. Pure cultures were also taken from croupous plaques of the mucus membrane of the vagina in a case in the typhoid period.

The results obtained in stools sent from the Isolation Hospital and gathered with due care also agreed with clinical observations always.

Results may become less accurate if the stools are kept for some time but that does not disprove the value of bacteriological examination. This is a delicate process and easily influenced by carelessness as to detail, such as having the wrong reaction in culture media.

The constant presence of the comma bacillus in the intestine and stools of cholera patients, is by now so well established that if contradictory results are obtained either errors of bacteriological technique or a wrong clinical diagnosis should be thought of in the first place.

The hypothesis of cholera symptoms caused by eating food contaminated by cholera bacilli allowed to pullate before cooking may account for one or another negative result. This should have the same effect as swallowing sterilized cultures, that is produce symptoms but make cultures impossible. Microscopic examination might also be impaired by the killing and subsequent alteration of the bacilli.

Symptoms similar to cholera may be caused by other microorganisms. Such symptoms were observed in two cases of poisoning, one of them with fish and the other with meat. At the Immigrants' Hostel 2,000 out 5,000 immigrants became ill simultaneously, on Christmas Eve, with vomiting and diarrhoea. Six hours before, they had all eaten salt cod-fish that had been soaked for 24 hours in rather impure water, during a hot spell. Twenty hours later almost all had recovered, though some were still very low, but one died, Post-mortem showed a condition different to cholera, without exsiccation of the tissues. Some of the stools were examined. They were rather like those of cholera but the mucous flakes were larger and contained more blood-cells.

In the other case, a father and son were taken ill after eating a head of pork, of which other members of the family did not partake. Both vomited violently and became very prostrate. The father's stools were sero-sanguinolent and showed large flakes of mucus, without feculent or bilious substance. The cultures were negative. The patients had no tenesmus and recovered next day.

This report was handed in two months late at the end of the epidemic, which may fortunately, now be considered as over."
Report for 1895: "Vibrios"

"The cases of cholera observed this year were mentioned in the last report. Cultures were sent to Prof. Dunbar, Director of the Institute of Hygiene at Hamburg, who is considered an authority on vibrios. The two cultures sent him by me as of cholera gave the Pfeiffer reaction, thus proving diagnosis to be correct. A third culture of vibrios, considered different to cholera, did not give the reaction, also confirming my view."

Excerpts from the Correspondence between Lutz and Prof. Dunbar (1):
Letter from Dr. Lutz written Febr. 7, 1895.
(Four specimens were sent).

"N. 1 labelled Cholera bacilli are cultures from a case examined during the last epidemic. They are identical with those of the first epidemic in all essentials. We have found these bacilli constantly, in both epidemics, and personally I have not the slightest doubt as to their specificity. It would, however, be useful to me to have a written statement from you to the effect that you have examined them and consider them as cholera vibrios.

N.° 2 Vibrios (not cultures) from a cholera diarrhoea I contracted in the laboratory by handling improperly packed stools.

N.° 3 labelled Vibrio morrhuae, which does not liquify gelatine and does not seem pathogenic. It was isolated from salt and dried cod-fish.

N.° 4 is another species, more closely allied to the vibrio of cholera and does liquify gelatine. It comes from the stool of a patient with a complex of symptoms somewhat like cholera but certainly due to eating cod-fish that had macerated too long. Its presence in the stools can be considered as accidental. This vibrio first produced a brick-red pigment in the more central parts of cultures, on different media, but soon lost this property. The stab-culture on gelatine looks like a water-spout and the screwlike whorls of the lower parts of the funnel are particularity noticeable. This vibrio was isolated by my assistant, Dr. Mendonça, under my supervision, and the other by me. We have been unable to identify them with described forms. They do not always, or in every medium appear clearly curved, but must belong to Vibrio or Spirillum all the same."

To these items Prof. Dunbar replied in his letter of May 24, 1895 as follows:

"As to culture N.° 1, I can only agree with your view that they are cholera vibrios. The colonies are fairly typical but liquefaction of gelatine begins slowly in them. Their reaction to Pfeiffer’s specific cholera test is entirely positive.

(For the full text see the Portuguese text and the originals annexed to it).
The same applies to culture from your own vibrio N.° 2.

Culture 3 Vibrio morrhuae arrived dead.

Culture 4 we also found to be different from Koch's vibrio in most points. It will interest you to know that it is quite negative as to Pfeiffer's serum test”.

REPORT FOR 1896: "CHOLERA AND CHOLERIFORM ENTERITIS"

"This year there was no epidemic of cholera. The few suspicious cases submitted for bacteriological examination proved to be cholera nostras and did not show the specific vibrio of asiatic cholera.

An increase of intestinal disorders, coinciding with a spell of hot and dry weather was twice observed. Various kinds of disorders were seen. There were many cases of diarrhoea, ranging from light to most severe, with symptoms of cholera nostras. Other patients showed symptoms of dysentery, also ranging from benign to severe and extremely severe. These disorders became almost epidemic, and undoubtedly seemed dependent on meteorological conditions, though it is difficult to say whether the influence of heat on food-stuffs or its influence on drinking water should be blamed. Several facts would indicate that the quality of water is impaired by hot and dry weather. It must not be forgotten that springs are not led immediately into conduit-pipes but gathered into large open reservoirs.

Some food-stuffs, like milk and meat, however, also deteriorate rapidly in this kind of weather. It is much to be desired that cold storage should become general the more so as very pure ice, almost free from germs, is now available".

REPORT FOR 1897: "ASIATIC CHOLERA AND CHOLERA NOSTRAS"

"There were no cases of cholera in 1897. In the one case of enteritis, submitted (April 3rd), the stools were completely discoloured and composed of serous liquid and yellow-white flakes of mucus, of different sizes, but generally larger than those seen in most of the severe cases of asiatic cholera. Several germs were found but not the cholera vibrio. Cultures also remained free from it. Though the case was severe, the patient recovered and the disease was classified as cholera nostras."

NOTE: Asiatic cholera did not occur again during Dr. Lutz' tenure of office, but vigilance was maintained unceasingly, so much so that the Report for 1908 (by Dr. Meyer), mentions that the Director of the Institute went to Jacarehy to see cases with symptoms similar to those of cholera and that they proved to be merely Cholera nostras.