

CHOLERA

Some Historical Reflections

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"Those who cannot remember the past are condemned to repeat it". — Santayana.

Introduction

It seems only a short time ago that, in order to bring my knowledge of tropical diseases up to date, I bought my third copy of Manson-Bahr's book on Tropical Diseases, as befitted an army man liable to see service in foreign lands, and a pathologist to boot who would have to think of exotic diseases when confronted with the duties, responsibilities and problems met with in the Armed Forces Medical Services.

Yesterday I had occasion, while trying to put my study-room in some sort of order, to take down from its customary prominent place in my meagre medical library my dogeared copy of this justly world famous reference book which happens to be the 15th edition, reprinted in 1961 from the 1960 edition; and as I thumbed my way through the various sections and their constituent chapters my fingers chanced to stop on chapter 31 — Cholera.

Now cholera has been one of the biggest, if not the biggest, public health problem that the World Health Organisation had to tackle in 1971-72, and medical interest in this disease which had stagnated so much during my years of medical studentship, and even in my post-graduate days, has had perforce to be rekindled and reviewed and indeed forced to make rapid advances when that notorious rogue variant the El Tor Vibrio quite unexpectedly in 1961 sprung its prison boundary in the island of Sulawesi and relentlessly made its way not only through the semi-dormant Asian continent catching many

countries therein unawares, but even succeeded in leap-frogging to the virgin ground of the Dark continent by 1971-1972, taking Europe through its southern flank en passant.

And these were the thoughts that floated nebulously through the labyrinthine recesses of my mind, as I pensively held Manson-Bahr in my grasp.

Etiology

I quote from page 31: 'The cholera vibrio was first discovered by Koch in Egypt in 1883; this he confirmed in Calcutta in 1884 by finding it in every case of the disease examined'.

As everyone agrees, this was an excellent piece of research, as was to be expected from that immortal master, with the French team, in the unavoidable absence, due to ill-health, of the equally immortal Pasteur, made up of Pasteur's best pupils' acting as a pace maker in Egypt, but it would appear that some merited honour even at this late hour should be given to the Italian Pacini who during the 1854 cholera epidemic in Florence detected the motile vibrios in the faeces of cholera patients and not only described their general morphological appearances but also correctly attributed an etiological relationship to the "immense number of vibriosis which I have found in the distended intestines'.

Pathology

'The cholera endotoxin causes a superficial denudation of epithelium, and increases its permeability; so that there is

a great outpouring of water and electrolytes with loss of fluid from the tissue and the blood' reads a statement on page 435.

By work on living specimens, involving the manipulation of elaborate gadgets like Crosby capsules it can be shown nowadays, both macroscopically and microscopically, that in cholera the patient's intestinal epithelium is more or less normal; which statement physiologists injecting some fashionable highly artificial laboratory macro-molecule like ^{131}I -PVP into a patient's circulation hasten to confirm in their turn.

Cohnheim lecturing a century ago told his students that "in order to understand cholera it is indispensable that we should possess an accurate acquaintance with the mechanism and processes on which the discharge of fluid into the intestinal canal depends. Naturally, it was at first hoped that the desired information might be obtained by an accurate examination of the intestine, the locality affected by the disease; but it was found to present no well-marked pathologico-anatomical changes. Nor is microscopic examination of any avail. One fact it is true, and that a very striking one, is revealed by the microscope, namely a deficiency of the intestinal epithelium. In the intestinal fluid there float, as a rule, quantities of epithelial shreds, both single cells and more especially connected cell-groups, some being pretty long membranous pieces of epithelium. This extensive shedding of the epithelium was formerly regarded as, and is still held by many to be, the criterion distinguishing cholera from other acute diseases of the intestine accompanied by diarrhoea, to be, so as to speak, the anatomical basis of the disease. But is the desquamation really a pathological process? All speculation is rendered superfluous in cholera by the ease with which the intestinal contents may be examined with the greatest accuracy *intra-vitam*; for if the epithelium is shed during the attack we must necessarily find it in a corresponding amount in the dejections. Yet, however often and confidently its discovery in the stools has been asserted, this is not the case. During the epidemic of 1866, many hundreds of rice-water stools were

examined in the various cholera lazarettos of Berlin by Kuhne, Bruberger, Hirschberg, myself and others; but although we all directed our attention especially to the presence of epithelium we only rarely succeeded in finding a few undoubted epithelial cells therein; and even with regard to these it was not possible to exclude absolutely an accidental contamination. Accordingly, there cannot, in my opinion, be a doubt that the entire desquamation of the epithelium is nothing but a result of post-mortem maceration."

Pathophysiology

I read on, 'Vibrios do not apparently produce any exotoxin. The endotoxin results from the destruction of the vibrios within the bowel lumen' (vide page 434).

Mainly through the impetus of renewed medical interest in cholera, resulting directly from the current 7th Pandemic, it has been discovered, without a shadow of doubt, that the vibrios do in fact secrete an exotoxin(s) (Cholera: Diarrhoeal Factor: Permeability Factor) which stimulates the enzyme adenylcyclase sited on the surface of the epithelial cells (and possibly located inside the cells as well) to trigger off a mechanism leading to the profuse watery gut contents, so characteristic of florid cholera.

Was this what that genius John Snow had in mind, albeit chemically-speaking not so word-perfect, not ten but one hundred years ago, when he opined, 'From all that I have been able to learn of cholera, both from observations and the descriptions of others, I conclude that cholera invariably commences with the affection of the alimentary canal. It follows that the morbid material producing cholera must be introduced into the alimentary canal; and the increase of the morbid material or cholera poison must take place in the interior of the stomach and bowels.

It would seem that the cholera poison, when reproduced in sufficient quantity acts as an irritant on the surface of the stomach and intestines, or what is still more probable, it withdraws fluid from the blood circulating in the capillaries, by a process

analogous to that by which the epithelial cells of the various organs abstract the different secretions of the healthy body.

Treatment

I thought that page 442 summarises very well the lifesaving treatment as practised today. I quote, 'Maintenance of biochemical equilibrium:- these measures are

- (1) Replacement of fluids.
- (2) Maintenance of blood and tissue chlorides at their natural levels.
- (3) Counteraction of acidosis.

Intravenous salines:— In the stage of collapse, which is due to the loss of a large amount of fluid, intravenous injections of salines must be resorted to, to restore the balance. Three to four pints may be necessary. The modern drip transfusion method should be used whenever possible.

It is assumed that in this day and age every medically qualified man (and para-medical personnel as well) is familiar with the recommended treatment of cholera, which, as stated above in Manson-Bahr, is the immediate introduction into the human body of fluid/electrolyte replacements. This vital procedure rapidly corrects the hypovolaemia, restores the lost ions, and neutralises the acidosis.

But lest our younger medical colleagues, perhaps not as well acquainted with medical history as they should be, should think that this is indeed a marvelously modern method of bio-physical therapeutic resuscitation, let them hark back to John Snow (1894): 'It is only necessary to allude to the effects of a weak saline solution injected into the veins in the stage of collapse. The shrunken skin becomes filled out, and loses its coldness and lividity; the countenance assumes a natural aspect; the patient is able to sit up, and for a time seems well. If the symptoms were caused by a poison circulating in the blood it is impossible that they should be suspended by an injection of warm water, holding a little carbonate in solution. The whole quantity of fluid that requires to be effused into the stomach and bowels, in order to reduce the

blood of a healthy adult individual to the condition in which it is met in the collapse of cholera is, on the average, 100 ounces or 5 imperial pints. This calculation may be useful as indicating the amount of fluid which ought not to be exceeded in the injection of blood vessels'. And I daresay one or the other of my Scottish confreres would demand redress on a matter of national pride and prestige if I do not reproduce hereunder at least a paraphrase of the following relevant document.

Malignant Cholera

Letter from Dr. Latta to the Secretary of the Central Board of Health, London, affording a view of the Rationale and Results of his Practice in the Treatment of Cholera by Aqueous and Saline Injections:

Leith, May 23, 1832.

Sir,

My friend Dr. Lewins has communicated to me your wish for a detailed account of my method of treating cholera by saline injection into the veins.

I have no doubt that it will be found, when judiciously applied, to be one of the most powerful, and one of the safest remedies yet used in the second stage of cholera, or that hopeless state of collapse to which the system is reduced.

I beg leave to premise that the plan which I have put in practice was suggested to me on reading in 'The Lancet' the review of Dr. O'Shaughnessy's report on the chemical pathology of malignant cholera, by which it appears that in that disease there is a very great deficiency both of water and saline matter in the blood.

So as soon as I learnt the result of Dr. O'Shaughnessy's analysis I attempted to restore the blood to its natural state. I resolved to throw the fluid immediately into the circulation. In this, having no precedent to direct me, I proceeded with much caution. I dissolved from two to three drachmas of muriate of soda and two scruples of the subcarbonate of Soda in 6 pints of water and injected it at a temperature of 112°F.

As soon as the pulse fails again, or the features again shrink the venous injection must be repeated, taking care that the fluid in use retains its proper temperature.

The quantity to be injected depends on the effect produced, and the repetition on the demands of the system, which generally vary according to the violence of the diarrhoea; the greater the degree of collapse, the greater will be the quantity needed.

The apparatus I have used is Read's patent syringe, having a small silver tube

attached to the extremity of the flexible injecting tube. The syringe must be quite perfect, so as to avoid the risk of injecting air.

I am Sir,
your most obedient Servant,
Thomas Latta, M.D.

Oscar Felsenfeld has well said that "It is natural that most logical brains follow similar pathways, and newcomers in the field will sooner or later follow the trek that was travelled by the old".