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Cy. 1

The Variability of Dysentery Bacteria in the Light of New Research.

by
Dr. Friedrich Hoder.

Whoever has once had the occasion to be concerned, in a research institution, with the bacteiological diagnosis, knows the numerous cases of intestinal infections whose etiology often introduces difficult bacteriological questions. In a typhoid stool, which contains a sufficiently large number of typhoid bacilli, the causative agents of the disease are easily and certainly found. This holds true for paratyphoid, for dysentery, assuming that the discharge is sufficiently fresh and the bacteria still living. Thus in as far as typical disease case are considered and typical bacteria with incontestable identifying marks are chosen from the research material, the work of the bacteriologist is purely schematic, simple and attended by success. If the investigation is definitely negative, then the work of the bacteriologist, in the individual case is discharged. This is not true, however, if he finds germs whose felationship to a sharply limited and characteristic group of disease agents can not be directly determined. These kinds of cases, which are very numerous, and in the presence of which the research must be assisted by difficult diagnoses (Bart once said, in one such case, the good conscience of the bacteriologist decides), is cleared of the inadequacy of our technique and methodology.

Already the division, which is necessary on practical grounds, of intestinal bacteria into pathogenic and apathogenic groups is scientifically only correctly limited. Thus one can say approximately that the bacteria of a given group are mostly pathogenic while most of another group are apathogenic. Typical typhoid bacilli are probably

also pathogenic in reaction. In the case of paratyphoid in contrast, the question of pathogenicity assumes indeed a very different form. Sufficiently often one can isolate typical paratyphoid bacilli from the intestinal contents of healthy men or animals without the carrier having been sick at any time or becoming ill in spite of the germs which they carry. Dysentery bacilli, in return, will usually, but in no ways always, produce the specific disease and RUTSCHKO recently said frankly that the orifinal germ for all dysentery types is a semiparasite which lives in epidemic free intervals in the intestine of healthy men. The bacteria of the coli group after all are in general apathogenic intestinal inhabitants. How little the facts tell is generally known.

This holds true for the definite boundary of individual groups, which were artificially made, again from practical bases. We know of changes from one group to others which could be arranged and characterized only with difficulty, especially since they are generally found in a state of variability. They are apparently also of constant form, however, which occupy intermediate areas of the so called Paracoli between the common coli and paratyphoid.

The cause of the bacteriol variability lies in part probably in the structure of the bacteria of which we naturally know very little. In part they are determined by external moments which are chiefly to be looked for in injury and irritating effects respectively of the bacterial cells. Thus approximate age of the cultures, action of substances which are irritating in a given concentration but which cause death at another(as for example, disinfectants, and not last, the best studied variation-producing agent, the D'Herelle's Bacteriophage.)

Since the causes of the bacteria variation which we know and

which made it possible for use to produce voluntary variants in a reagent glass only exhibit a slight fraction of that influence, to which the germs in nature displayed are obvious. First of all, once a bacterium is already in its natural environment and under natural living conditions, for example, a typhoid bacillus in human intestine, it is under conditions completely different from those of the corresponding culture strain. Then however the processes in the body, in our case, the intestine, are naturally more complicated than we could produce in a reagent glass. What happens to the bacterium in the organism, of what sort are the modelling influences of the environment on the germs, could we preserve the highest and deduce theories for our presemtions. Also we do not know anything, with any exactness about these influences.

Especially interesting studies, which in the course of the last years at our Institute were carried out by Rutschko, and Rutschko and Hilde Hoder, are appropriate for returning the problem of bacteria variation again to the foreground of interest.

Rutschko had earlier shown that in the discharges of men sick with dysentery not a single dysentery type, but on the contrary more than one type was present. He succeeded in proving this in 15.5% of 218 positive dysentery cases and indeed he observed the simultaneous appearance of more types usually at the conclusion of the sickness, besides in reactions in chronic cases and in the case of bacilli carriers. This determination, as interesting as it is important, is based on the investigation of different colonies on the inoculation of a stool probe. In general Rutschko found about as many different kinds

of dysentery as colonies which he studied.

For example, the percentage rate of dividing more dysentery types in the stool in the case of a test of more colonies was as follows: With investigation of 5 colonies 11,9%, with study of 10 colonies 24%.

The investigation of only 1-3 colonies, as is done generally in practice must according to Rutschko, lead to misleading results in relation to the number of types of dysentery bacilli present in the case of persons ill with dysentery and bacilli carriers.

There are only two explanations for the simultaneous appearance of different dysentery types in this kind of discharge. Either the ill were simultaneously infected with the different types or the germs changed in the human organism. The first suggestion is so improbable that only the second appears discussible.

Rutschko produced the experimental corroboration for the gradual transfer of one dysentery type into the others by feeding studies with hens and cats and Rutschko and Hilde Hoder did it for monkeys. An animal which was fed a determined uniform strain(also strains, which came from single cultures, resulted in the same result) furnished different dysentery types in stools.

The question about the cause of the change naturally remain open. How large a role the bacteriophages, which accofding to the infection in the discharges of animals were demonstrable, have in the germ vatiation, we do not know. However, since the bacteriophages in vitro have an extraordinarily strong mutation producing influence and also in view of the apparently spontaneous changing of the dysentery bacteria

in the cultures in the presence of lysinogenic strains which could be of significances in producing deviation(Hoder and Krebelianowich), the analogous conclusion, that they function also in vitro in a corresponding manner, is not known offhand. Along with the bacteriophages, however, a great number of factors without doubt play a role in the living organism about which we know almost nothing.

According to Rutschiko the Bacterium Shiga Kruse under laboratory conditions can change into each dysentery type, except the Schmitz-Stutzer. In contrast, he did not succeed in changing other dysentery types into the Shiga strains, if he also retained the more frequent variants, which were very close to the genuine Shiga. The greatest transfer into other forms of dysentery fell in the Flexner-Y group. According to Rutschko there are stable and variable types of dysentery. If an epidemic stems from a stable form, then one will find only one type of dysentery in the stool of the ill, in other cases however, new types were always arising by continuing change and were demonstrable. Rutschko excluded the results of his studies since the Bacillus Shiga' Kruse Sonve or a type very similar to it which lives as a semi-parasite in the intestines of healthy men during epidemic free intervals, since the initial type of all dysentery bacilli can be considered such a type. He can increase in virulence from hitherto completely unknown causes, he can produce disease and then vary under the varied conditions in the deseased organism and under the effect of bacteriophage its biochemical and serological relations inorder to transfer it into other types of dysentery.

Of especial interest are in addition the investigations of

Rutschke and Hilde Hoder in monkeys, The discharges of some healthy monkeys had been thoroughly studied for a long time before the start of the study so that their normal intestinal flora was very exactly known. The authors then fed these monkeys dysentery bacilli and observed, in addition to the already discribed change over of germs which were red, into other types which differed from the original strains, the appearance of colonies in the stool smears of the animals, which they must consider on the basis of key typical appearance, as dysentery colonies, and which with the case of the following cultural investigation are in the many colored series. as are also considered typical dysentery and could be classified randomly as different types. After several days to weeks, however, the authors noticed in the pure cultures the appearance of gas formation in the sugar nutritive substratum and a new study showed the existence of coli at the place of dysentery bacteria. We are thus dealing with, in these strains obviously because of the changed coli germs, which occurred in the intestine of the animal under the influence of the infection, possibly also under the influence of bacteriophages and corresponded in their relations to the dysentery bacteria. Gas, indole forming capacity and flexibility disappeared - a phenomenon , which furthermore has been repeatedly observed in the presence of coli also in the reagent glass with and without the action of bacteriophages — and the sugar splitting ability was changed in such a way that the identification with dysentery germs was carried out without doubt, in cases where it had dealt with simple diagnostic studies as undertaken in recent centers, and the strains had not been

observed and controlled constantly. These results are extraordinarily important as they throw light on the possibility of the eventual origin of dysentery similar bacteria from common Bact. Coli.

The sharp limit of the so-called coli group from the above groups of the intestinal parasite has already become illusory by the numerous investigations of many authors on the variation of the intestinal bacteria. I draw attention only to the continuous change of common coli to the Paratyphoid group, which we obtained by the action of specific bacteriophages, and further to paratyphoid like germs which grow on very different media, which could be changed back by repeated passage on Litmus milksugar agar and dienoculation of suitable reactions in part into common coli(Hoder,Hoder and Susuki, Singer and Hoder). The germs before the appearance of the reactions differed neither culturally nor seriologically from bacteria of the Fleischvergifter(meat poisoning) group. They finally emerged however as derivatives of common coli. The reverse change naturally did not succeed in all cases. Obviously the qualities of such a modified coli strain, if the study succeeds is, as a rule stablizing for a long time, that is to say, new kinds arise and only then when one accidentally pushed from a still relatively labile form, the separation of reaction which succeeds in revealing the origin of the unclassified strain.

According to the studies of Rutschko and Hilda Hoder, bacteria similar to those of dysentery also appear.which however the unbiased observer must consider unconditionally as true dysentery strains when he does'nt observe the germs during a long time-span and must repeat often his study,under determined conditions at least in the intestine of infected animals in order to know to distinguish them from coli strains.

The conclusion that they are likewise cultivated in the human intestine under the influence of more or less turbulent courses of disease, which was missing in the monkeys, likewise is approximately correct. How far the attributes of such a strain could become stabilised so that no throwback appears, may remain undecided.

From these infestigational results it follows with compelling clarity how necessary it is to be the most severe critic in the judgment of apparently perfectly unobjectionable and typical agents of disease, which are raised from embedded material of a study preparation. An enteritis, perhaps harmless in itself can under certain circumstances be considered as severe dysentery. That is, especially the healing success in such cases scarcely may fail to appear, probably seemingly unimportant for the therapy, but not for the patient, who is teased unnecessarily by isolation and comparable precautions.

The very extensive morphological variations of the gram negative intestinal bacteria in general and especially the dysentery bacilli which chiefly by the surprisingly stimulating study of Ph.Kuhns and his pupils have returned to the foreground of interest of greater importance for the epidemological research. The Kuhn's Pettenkofer(test) appears not only in pure cultures in vitro; it could also, as Rutschke repeatedly observed likewise exist in the intestine and in the same way occasion false diagnosis. If a dysentery bacillus appears in cocci-form and is atypical then it is natural to at least manifestly deny its membership in the dysentery group. Such cases also occasion false diagnoses and

in additional series under certain circumstances occasion surprising results of apparent germ change when one such strain is accidentally studied further.

Provided that the theory of the existence of a cycle of change of bacteria(Kuhn and his pupils and recently Rutschko) should be verified and numerous studies supporting it, then this would indeed be a considerable step forward in bacteriological research and bring new possibility of getting nearer the solution of epidemiological problems, but also at the same time it would signify a great complication for applied bacteriology.