enteritis bacilli occur frequently in flies in the natural state, and that the utmost care is necessary in discriminating between these and the true enteritis-producing organisms.

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The Croonian Lectures

ON

ADAPTATION AND DISEASE.

DELIVERED AT THE ROYAL COLLEGE OF PHYSICIANS, JUNE 21ST, 1917.

BY J. G. ADAMI, M.D., F.R.S.,
LIEUT.-COLONEL C.A.M.C.

LECTURE III.

ADAPTATION TO DISEASE-PRODUCING AGENCIES IN THE HIGHER ANIMALS.

(*Abstract.*)

FROM the data brought forward thus far the following conclusions can reasonably be drawn:

1. The evidence is abundant and conclusive that bacteria are capable of being modified by alterations of environment of certain orders.
2. The modifications conform with Herbert Spencer's "direct adaptations."
3. It can be shown that not some, but all, the microbes subjected to particular orders of alteration of environment exhibit the particular modifications: the hypothesis of "chance variation" in one direction with survival of the fittest is incapable of explaining the phenomena.

After calling attention to two examples of direct adaptation in protozoa higher than the bacteria, namely, the conversion of negative into positive chemiotaxis in the myxomycete, Fuligo, and Musgrave and Clegg's observations upon the accustomance of entamoebae from the intestine to new bacterial and tissue foodstuffs, it was pointed out that the overwhelming studies of the last quarter of a century upon immunity afford the deepest insight into the processes involved in direct adaptation in the higher animals. There is a vast literature upon the subject. Some of the most notable achievements in science of our generation have been in this particular province. The names of Pasteur, Koch, Ehrlich, Metchnikoff, Almroth Wright, are household words. Every intelligent being knows something about tuberculin, diphtheria antitoxin, phagocytosis, and typhoid inoculation. Yet no single general biologist has dealt seriously with the significance of these discoveries in relationship to adaptation and evolution.

Typical examples were afforded demonstrating that immunization of the individual is direct adaptation. The cases of the phytotoxins, abrin and ricin, were considered in the first place. Both are intensely poisonous in minute doses. Against both the animals of the laboratory can be immunized so that they can withstand 500 or 5,000 times the lethal dose; the blood serum of the immunized animals contains bodies which neutralize the toxin. Evidence was given showing that the cells of the body of the immunized animals elaborate and discharge the antitoxin in great excess over the amount of toxin originally introduced; that they continue to elaborate this for weeks and months after the introduction of the toxin. We deal with the acquirement of a new property which cannot possibly be regarded as the calling into activity of a property previously possessed; the acquirement is something positive; there can be no alternative hypothesis of loss of inhibiting factors; no possibility of ascribing the new property to the persistence of a chance variation. Antiricin can be produced in rabbit or mouse with absolute certainty, and there is here no alternative explanation of the survival of the fittest.

The parallel examples of the production of diphtheria and tetanus antitoxins were then taken up, and next it was shown that the cells which absorb and fix the toxins produce the antitoxins. Following this, the more widespread bacteriolytic immunity developed against members of the typhoid-coli group, cholera spirilla, micrococci, etc., was studied and shown to be an acquired power of digestion of unfamiliar proteins, especial reference being made to Pfeiffer's reaction. Nor is the acquirement of necessity temporary in the individual. It may last for months and even years. Reference was made to the agglutinating powers of the blood of those recovered from typhoid fever months and sometimes years after complete convalescence.

This continued production exemplifies what Weigert and Fraser Harris had referred to as the "law of inertia." In the order of events here discussed the lecturer held that the activity once started continued too long to be comparable with physical inertia or momentum; there seemed to be the setting in motion of a serial or cyclic series of intercellular reactions and counter-actions, the one action starting the other. He preferred, therefore, to employ for the present the non-committal term of "the law of habit."

Numerous examples were given of the working of this law of habit in association with morbid states of various orders in man, of the survival of symptoms long after the agent causing the symptoms had disappeared, particular reference being made to the tics, hysterical and neurotic manifestations; the continued production of antitoxins and bacteriolysins was of the same order; he held that this same law explained the metaplasias and neoplasias.

As to the *inheritance* of these acquired conditions in the higher animals, he pointed out the restrictions induced by conjugation and amphimixis, the difficulties introduced in mammals by the intrauterine existence of the fetus, and in man by social customs. Two conditions have to be taken into account—namely, those of indirect and direct (or identical) inheritance.

Regarding indirect inheritance, it has to be observed that the germ cells are not so sacrosanct as to be insusceptible to influences affecting the body at large. The germ cells have to absorb foods and grow. If the lymph contain soluble substances the germ cells are not precluded from absorbing and being affected by them. And that this does occur is well shown by the studies upon the effects of paternal intoxication with lead, mercury nitrate, products of the tubercle bacillus, abrin, etc., the mother not being exposed to the poisons. In all these cases reduction in the number of pregnancies is noted, with increase in the number of stillbirths, liability to death within a few days after birth, and the production of an impoverished and highly susceptible offspring, but a small proportion of the progeny reaching maturity. Lustig and Watson (with abrin), Carrière (with tuberculin) note, in addition, an increased susceptibility on the part of the offspring towards the specific poison.

Of all these observations the most clear and decisive are those of Professor Stockard, of Cornell University. He subjected male guinea-pigs daily for a period to the fumes of alcohol, and mating them with normal females obtained but five living litters from twenty-four matings, and of the twelve offspring, seven died in convulsions soon after birth; the survivors, when two months old, were half the size of control guinea-pigs of the same age. When now the nervous and undersized members of this second generation were mated, even when unrelated and never themselves exposed to alcohol, their offspring tended to be still more degenerate, and to show gross deformities. Mating together unrelated members of this third generation, in the few examples observed, gave even more unfavourable results. In other words, two alcoholized great-grandfathers influenced the progeny down to the fourth generation.

We have here the most precise evidence of the inheritance of acquired defects, evidence that fits in wholly with our routine medical experience of the danger of marriage in families which exhibit like nervous or other defects. With these experiments before us it is absurd to postulate that defects of these orders are atavistic, due to properties

which have been always possessed by some one or other strain introduced into the family. We must recognize that infection of one or other order, and intoxication, are capable of telling upon the parental germ plasm, and are capable of leading to the acquirement of conditions of defect. To us as medical men it is a minor point whether there is inheritance of the exact defect seen in the parent primarily subjected to the particular influence. At the same time it is not a little interesting that alcohol, lead, and bacterial toxins particularly affect the nervous system in the adult or adolescent, and that these acquired defects are peculiarly liable to influence the nervous system in the offspring.

"Parallel induction" of defects in body and germ cells have been noted of later years, and are being accepted, by an increasing number of zoologists and botanists interested in experimental embryology. The recent work of Kammerer upon *Salamandra maculosa* was cited in this connexion.

Instances of direct inheritance of acquirements are, and must be, rare and limited to cases in which the influences which, affecting the body cells, modify their internal secretions, and through these internal secretions so tell upon the germ cells and their metabolism as to set up similar defects and similar disorders of the internal secretions in the offspring. We know, as a matter of fact, that the endocrine organs as a class have a profound influence upon the generative organs and upon growth, and, from general experience, that metabolic disorders—gouty and "rheumatoid" states, defect and excess of internal secretions—are heritable. The results of medical research strongly support Darwin's earlier contention that congenital variation is to be attributed to the action or influence of changed conditions upon the parental body, and through it upon the reproductive germs. At the same time they indicate the existence of a limited group of cases in which the Lamarckian principle is exemplified, namely, that of identical inheritance of conditions acquired by the parent.

Thus at length, after long years of vague wanderings in the wilderness with not a little heavy fighting, we have, if mixed metaphors be permitted, conquered our Vimy Ridge, and although for a time held up, can indulge in a Pisgah view, and see when and how the next advance is to be made.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

A CASE OF ENTEROSPASM.

I HAVE read with interest the article by C. H. Whiteford, in the JOURNAL of March 24th, entitled "A case of enterospasm in which the portion of intestine involved was of unusual extent." In the *Middlesex Hospital Journal* for October, 1916, I recorded a case of enterospasm in a boy of 18.

This patient was suddenly seized with acute pain in the epigastrium while at tea, and, on examination, I found him to be suffering from profound shock, with a pulse rate of 120, temperature 99°, and abdominal distension. A history of attacks of acute indigestion during the past two years was obtained. An examination of the abdomen revealed absence of liver dullness and immobility of the muscles of the anterior abdominal wall on respiration. There had been no vomiting. As it was considered possible that some abdominal catastrophe had taken place, it was decided to perform an exploratory operation without delay. On opening the abdomen in the middle line, immediately above the umbilicus, distended coils of intestine forced their way through the wound. An examination of the small gut showed that some portions were collapsed, simulating the condition found in the intestine distal to a mechanical obstruction, while other portions were dilated. No evidence of blockage of the lumen of the gut was discovered. The stomach was dilated, and the gall bladder distended to the size of a "William" pear. As the condition of the viscera was considered to be due to a functional lesion rather than an organic one, it was decided that further operative interference was inadvisable.

The day following the operation the patient commenced to vomit pure bile in large quantities. The vomiting lasted for twenty-four hours. The pulse-rate, previously maintained at over 100, decreased, and the abdominal distension gradually disappeared. Apart from considerable difficulty in getting the bowels to act, convalescence henceforth was uninterrupted.

Paresis of the duodenum probably accounted for the distension of the gall bladder and the biliary vomiting, following operation. It is possible that this vomiting might have been prevented had the gall bladder been aspirated.

As Dr. Whiteford points out in his article, these cases of enterospasm occur in neurotic subjects, but it is most likely that undigested and irritating foods, such as fruit seeds, may act as an exciting cause.

A. CLIFFORD MORSON,
Temporary Surgeon R.N.
H.M. Hospital Ship *Karapara*.

A METHOD OF PREPARING AND USING CATGUT.

IN this process the catgut is rolled, inserted in a tube containing the sterilizing solution, and the tube is closed so as to be air-tight. One lot of tubes are small, for ligation; the others about double the length, for suture. These tubes are controlled during operation by the surgeon, thus avoiding waste of time or material, as in the ordinary way of passage from attendant to surgeon, and the risk involved in such handling. The tubes are conveniently about 2 by 9 and 2 by 16 cm. long, with screw top, corks, and screw-on metal caps. The central part of the cap is removed, leaving just the peripheral portion. This arrangement prevents the corks coming out when the gut is drawn from the tubes. There are two suture tubes, one containing raw and the other chromic gut. The tubes are closed by cork or ether proof rubber stoppers.

The sterilizing solutions used for gut are ether, chloroform, absolute alcohol, or petrol. Any one of these is a powerful germicide and will render gut sterile in twenty-four hours. These have the great advantage, besides, of being volatile and therefore soon leave the catgut after withdrawal from the tube and before insertion of the gut into the tissues. Thus one or other of these substances satisfies a desideratum that I had been looking for in that it has the advantage of germicidal solutions (sterilization) without their serious disadvantage (retention in gut after removal with irritant action of contained chemical upon tissues). Another advance in the aseptic technique.

I have been using ether as the sterilizing solution of choice. This substance proves lethal to the ordinary pyogenic germs in a very short time, as I have demonstrated. All that is required to sterilize the gut is simply to insert it in ether and leave there indefinitely; it can safely be used after twenty-four hours, probably much sooner. In winding the gut reels are avoided, as they would take up too much space and render the glass tubes unnecessarily bulky to hold in the hand whilst working. The gut can be conveniently wound on a bandage roller. I use a nickel plated one with a thin rod carrying two circular discs to regulate any desired length of spindle; the spindle is to be long and thick enough to readily fit the tube. The end of the gut next the rod of the roller (that is, the commencing end) is left long, so that when the gut is drawn off the roller this end can be threaded through the cork by a straight needle, and the gut roll unwound from the core outward, the other end of the hank of gut ending on the outside of the spindle. This method of rolling takes up the minimum amount of space and enables the gut to be withdrawn readily. The ligature tubes contain one roll, the suture tubes about three rolls of different and convenient sizes. When the tubes are corked and the caps screwed on they are kept in an air-tight glass receptacle containing an antiseptic such as alcohol, petrol, etc., or an aqueous or spirituous solution of biniodide and sodium bicarbonate tablets, in which they remain immersed when not in use. For this purpose I use petrol, which is efficient and cheap, but its inflammable nature must not be forgotten. After using the tubes they are washed free of blood, etc., and replaced in the receptacle. The cap of the latter may be like those of the tubes (screw on). A container holding two long tubes and six small is convenient for carrying about, but larger ones would be required for hospital use. If non-volatile disinfectors are employed in the container the ordinary catgut jars may be used. The advantage of volatile solutions here also is that they evaporate, and therefore do not get on the hands to irritate the tissues.

As to the sterilization of the gut, the process is simplicity itself. Nothing else is required after rolling but