the case, however, the period of convalescence is fraught with considerable danger to life, and even in the most favourable cases is often protracted for several months, and not infrequently marked by serious relapses. Thus I find that among 100 consecutive cases of chronic gastro-intestinal catarrh in infants which have come under my care at the Evelina Hospital and elsewhere, no fewer than 24 died after the symptoms of the primary disease had apparently subsided. Of this number 13 succumbed to an attack of whooping-cough (9) or measles (4), 6 died either from broncho-pneumonia or tuberculosis, while the remaining 5 were subsequently attacked by acute intestinal catarrh, which proved rapidly fatal.

Another point of interest is to be found in the tardy and incomplete recovery which is made by some of the victims of the complaint, who remain thin and weakly for many years, and apt to suffer from attacks of subacute catarrh of the stomach or bowels from trivial causes. Even those children who apparently recover completely from the disease often exhibit a remarkably slow growth, and are apt to remain stunted in stature or backward in mental development for several years. These facts suggest a question as to how far chronic inflammation of the stomach and bowels in infancy can influence the digestive functions in adult life, and although I am not prepared as yet to answer this question in a decisive manner, there are yet a few facts in this connection which are worthy of consideration.

A few years ago, when engaged upon a microscopical examination of the digestive organs of persons who had died of various diseases, I was struck by the occasional appearance of small patches of cirrhosis in the mucous membrane of the stomach near the lesser curvature. I have since observed similar appearances in the stomachs of children whose history indicated that they had suffered from gastro-intestinal catarrh in infancy.

It has already been stated that catarrhal inflammation of the stomach seldom presents a uniform distribution, but that in certain districts, and notably in the pyloric region near the smaller curvature, the disease attains its fullest degree of development more speedily than elsewhere. And since after the second year of life the increase in the size of the stomach is chiefly confined to the fundus and along the line of the great curvature, it is obvious that should any relics of inflammatory mischief persist to adult life, they will be found in that part of the viscus which has undergone the least structural change, namely, the pyloric.

Lastly, there is a certain form of habitual dyspepsia in which the complaint invariably commences about the time that the body attains its full development. The victims of this troublesome disorder have almost always displayed an abnormally rapid growth after the age of puberty, and consequently the loss of digestive power is commonly ascribed to the phenomenon of "outgrowing the strength." But in many of these cases, at any rate, careful inquiry will elicit the fact that as a child the patient had always been puny and delicate, and had suffered severely from vomiting or diarrhoea. Putting these different facts together, it does not seem improbable that organic mischief wrought in the mucous membrane of the stomach in infancy may persist through the whole life, and exert a permanent and deleterious effect upon the functional activity of the organ should the requirements of the system expose it to exceptional strain.

The fact that the secretion of hydrochloric acid fails in cases of catarrh of the gastric mucous membrane affords a certain amount of help both in the diagnosis and prognosis of the chronic disease of infancy. In out-patient practice, where it is common to find extreme degrees of emaciation arising from criminal neglect, I have often found the stomach tube of the greatest value in checking the statements of parents and nurses, for by its help the stomach can be easily evacuated, and its contents submitted to immediate examination. Thus I have often demonstrated an absolutely empty stomach in an infant which was supposed to have recently enjoyed a full meal, or the presence in the organ of some article of adult diet the administration of which had just been strenuously denied. In these cases of starvation, also, the stomach, even when devoid of food, usually contains a small amount of fluid in which both hydrochloric acid and pepsin are present; and since the acid in a free state is seldom encountered in the

diseased condition of the organ, we have at our hand a ready method of distinguishing between cases of wasting of the body arising from want and that which results from disease. As an aid to prognosis the method is, perhaps, less valuable owing to the difficulty of performing an accurate examination of the gastric contents in ordinary practice. It may, however, be said that the reappearance of free acid in the stomach is a sure sign that, with ordinary care, the child will recover its flesh and strength. Even in those cases where free acid continues absent for a length of time, there is always hope as long as the contents of the organ after a test meal contain an excess of mucus, and possess an appreciable quantity of combined hydrochloric acid. In those chronic and severe cases, on the other hand, where the contents of the stomach hardly exhibit any acidity at all, and obvious dilatation of the organ exists with a marked diminution in the hæmoglobin of the blood, a fatal termination of the disease is the only one which can be expected.

REPORT ON INFECTION AND IMMUNITY.

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Owing to the difficulty of obtaining pure vaccine material and the impediment which at the outset confronts one when experimenting with this material, caused by the fact that practically only calves can be used for inoculation purposes, I have directed my attention to investigating the question as to whether animals which are not normally affected by a specific disease germ could not, under certain abnormal conditions, be rendered more or less susceptible. I hoped to overcome this difficulty by subjecting the animal to those general and local conditions which have been recognised as increasing the virulence of infection. I shall consider these conditions and their effects briefly under the headings of constitutional and local.

It has long been recognised that an infection may be rendered much more acute when complicated with the presence of another micro-organism. It was subsequently shown that the sterile products of other microbes could exert the same influence, and this knowledge has been taken advantage of for laboratory purposes in regaining or increasing the virulence of pathogenic micro-organisms. Thus streptococcus erysipelas when grown on our ordinary cultivation media frequently loses its pathogenicity, and as it no longer is able to give rise to reaction in rabbits, the possibility of its regaining its virulence by passage through animals is completely obviated. If, however, the rabbit receives at the same time an injection elsewhere of the sterilised products of bacillus prodigiosus or some other organism the microbe of erysipelas gives rise usually to marked local reaction at the point of inoculation, from which the organism may be easily obtained for further transmission through animals, the animal not infrequently succumbing to the disease which has thus been induced. The cultivation of the organism obtained from this first animal is now usually capable of setting up a local process in a fresh rabbit, but its power is still further increased when aided by the presence of the other microbe, the virulence of the erysipelas being also increased by this process. It has been shown that the products of quite a number of different organisms can exert this "summative" influence on the process of infection, while some well-defined chemical substances can even be used for this purpose, and these include some of our best known antiseptics. It is certain, however, that this is not a mere general constitutional influence which subjects the animal equally to all species of infection, but that it is quite specific in its working.

Thus it has been found that the products of certain microbes, when introduced into an infected animal tend to arrest the process and cure the animal, exerting what we may term a "dissipative" action as regards another pathogenic micro-organism. The explanation of this circumstance is in all probability to be ascribed to the interaction of the two sets of toxic products on the cells of the animal undergoing infection. Thus, if the effect on the cells of the sterile bacterial

product is such that the effect is superadded to that exerted by the specific products of the disease germ we have a summative action, the infective power of the pathogenic organism being increased; while if on the other hand the action exerted by the sterile bacterial products on the cells of the animal tends to antagonise that exerted by the specific disease germ, we have a dissipative action, the process of infection being rendered less acute or even abortive. How very complicated this interaction of the toxins on the cells of the animal may be is indicated where a rabbit is subjected to a mixed infection of anthrax and erysipelas. The animal frequently recovers from the anthrax infection which would otherwise have been fatal, but it has sometimes been observed that the animal succumbs to the erysipelas, no trace of anthrax being obtainable, although the streptococcus would not by itself be fatal to these animals. This would seem to indicate that while the products of the streptococcus tend to antagonise the effects of the anthrax, the effect of the latter toxin may be superadded to those of the streptococcus. It must be recognised accordingly that the action is a specific one, and that we must search for that special toxin which exerts this cumulative action in the case of each specific disease germ.

Guided by this fact that animals can be rendered more susceptible to infections to which they are normally subject, I have been experimenting to ascertain whether it might not be possible to render animals susceptible to infections to which they are normally refractory. That the principle is in all probability correct was indicated in my last report,¹ where I stated that animals could be infected with gonococcus material in such a way that a purulent discharge of the urethra can be set up, which endures for several weeks. The examination of this discharge indicated the presence of many pus organisms along with apparently the gonococcus. Since the products of *M. prodigiosus* and other toxins undoubtedly aid the process of infection with pus-producing organisms to which this animal is not normally very prone, it may perhaps be questioned if the same effect could be produced with a pure culture of the gonococcus. It must be remembered, however, that the profuse urethral discharge in the human subject seems to be invariably accompanied by the presence of these pus organisms, to which the pus formation is no doubt in great part to be ascribed. This very encouraging result led me to experiment in the same direction with vaccine material. The cultures and sterile products of *Bacillus prodigiosus*, *Bacillus tuberculosis* (tuberculin), *Bacillus malleus* (mallein), *Bacillus diphtheriae*, and other organisms have been used alone and in conjunction to attain this end. The results obtained, although indicating clearly an increased susceptibility of the animal to the infection, have not up to the present been of such a definite character as to permit of their yet being used for experimental purposes. Thus when we inoculate with vaccine material the mucous membrane of the upper eyelid of an animal, under the influence of other toxins, we frequently have distinct inflammation even with the production of ulceration, which may after a considerable time become very marked, due, however, in great part probably to the constant irritation of friction due to the movement of the eye. The primary lesion, however, is not so definite or so certain that much reliance could be placed on it as regards the question as to whether the inoculation of vaccine material had "taken" or failed. The effects of inoculation varied at different times, and it would appear that the best results were obtained with fresh material introduced in considerable quantity. These results, I think, indicate only that I have not yet discovered the special product which would exert its cumulative influence on the infection of vaccinia, and I hope to continue the investigation on these lines by experimenting with other substances.

Recent advances in our knowledge have rendered it probable that normally refractory animals may be rendered susceptible to infection by another method. It has been found by Roux and others that the vaccination of an animal with one disease may render it very much more susceptible to the toxin of another organism, and similar suggestive results have been obtained in other departments of bacteriology. It would appear, indeed, as if the constitution of an animal can be so altered by vaccination to a certain disease that it will react to

another disease like an animal of a different species. I have not yet, however, had an opportunity of extending the research in this direction.

The influence of local conditions in aiding infection have been observed chiefly when substances have been introduced into the tissues which apparently exerted a devitalising influence on the cells. That this is the most probable reason is shown by the fact that physical injury to the fixed cells, such as a bruise produced by a blow, will produce the same effect in aiding infection. If this explanation holds good, any means which abrogated the action of the living tissues locally ought to exert a similar influence; thus, if the germ were inoculated into a sponge which was introduced under the skin it should be able more readily to induce infection, and this I have found as a matter of fact is really the case. Unfortunately if other organisms obtain an entrance at the same time they are also able to multiply undisturbed and complicate the process by inducing a mixed infection. To avoid this disadvantage of the method (the entrance of foreign organisms) I have obtained the same result in a different way; a solution of sterile colloidal silica, prepared in the same way as Winogradsky recommended for the cultivation of his nitrifying organism, can be injected subcutaneously, and this becoming solid *in situ* on mixing with the animal fluids, provides a pervious sterile foreign body, in which the organism can multiply undisturbed by the surrounding tissues. It was observed in some cases that its action was not so marked as that exerted by the sponge, and this appeared to be due to the contractile force of the skin and tissues tending to compress the jelly into a very small compass. This difficulty was obviated, however, by making the injection into a loose fold of skin. The method of infection I now use is as follows: A sufficient quantity of a broth cultivation of the organism experimented with is injected subcutaneously, and, without removing the needle from the skin, the syringe is refilled with the colloidal silica, which is then at once injected. On the death of the animal a portion of the gelatinous silica can be introduced into a tube of broth, and this fluid used for inoculation of the second animal, a series of transmissions being thus carried out without risk of outside infection. This is an exceedingly effective and convenient method for increasing the virulence of pathogenic organisms, and should find useful application in the production of those virulent cultures which are requisite at present for the production of curative serums. It can, of course, be combined where necessary with the constitutional methods which tend to favour infection. This method, of course, could not be made use of until the organism experimented with had been obtained in a pure form, and therefore could not be utilised at present in my research.

REPORT ON THE EXCHANGE OF BLOOD GASES IN BRAIN AND MUSCLE DURING STATES OF REST AND ACTIVITY.

BY

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INTRODUCTORY.

FOUR years ago, in his Croonian Lecture at the Royal Society, A. Mosso¹ adduced evidence to show that the brain is a seat of active combustion. By a long series of thermometric observations, he has come to the conclusion² that the temperature of the brain is frequently higher than that of the rectum or even of aortic blood, and, moreover, that the temperature of the brain rises still higher when that organ is thrown into activity by direct stimulation or by drugs.

If his conclusions be correct, the formation of heat in the brain must be very great, in order to raise the temperature of the whole organ and of the blood which is constantly coursing through its substance and carrying away the heat, above the general temperature of the arterial blood.

Hitherto the formation of heat in nerve has been undemonstrable, even by the most delicate means (Rolleston³). The

¹ BRITISH MEDICAL JOURNAL, July 27th, 1895, p. 211.