EPIDEMIOLOGICAL SOCIETY.

ON IMMUNITY AND RESISTANCE AS FACTORS IN THE
EPIDEMICITY AND ENDEMICITY OF INFECTIVE
DISEASES.*By HERBERT E. DURHAM,
Grocers' Recess Scholar.

It may be laid down as an axiom that persons or animals which are harbouring the specific organisms of diseases affecting human beings are to be regarded as dangerous to the community. It may be likewise deduced that if such individuals are actually suffering from typical attacks of a given disease, they are more likely to be dealt with as such than if they are suffering from unrecognisable or unrecognised forms of the disease, and still more than those that are not suffering at all, although more or less infested with the causative agent of the disease.

In comparatively recent decades there was an optimistic belief that the "specific infective maladies were characterized by very definite adherence to type;" for it was not appreciated that a given infective agent might cause extremely different symptoms according to the nature of the individual infection. To take an example: an organism like the pneumococcus may give rise to a typical pneumonia, to an empyema, to an acute cerebro-spinal meningitis, or to an acute osteomyelitis, or to a purulent peritonitis, whilst each of these may demand special forms of clinical treatment; yet, so far as concerns their actual ætiology, they are one and the same disease. But, beside such differences, which are due to varied manner of manifestation, we have to recognise variations in intensity of attack. The intensity of attack depends upon two main factors, both of which are variable according to laws of which we have as yet but little knowledge. One of these factors is the variation in resistance of the host, the other is the variation of the infective agent; the latter may vary in its infective or resisting power, or in its power of poison-production, or, again, in both of these.

At present we are concerned with the variations in receptivity of the host; and with our scanty knowledge of the laws which govern the variations of the parasite, this side of the question may be left alone. It is well known that different individuals, varieties, and species vary considerably in their susceptibility to virulent organisms; they may be more or less refractory by nature, or they may have acquired a specific immunity, either by reason of the direct action of the agent upon them, or by reason of transmission of such acquired immunity in some degree from their mother (the transmission of the agent may also happen).

In any case, whether the proneness to resist infection be due to a non-specific resistance or to a specific immunity, it must be remembered that their powers are limited. We know of no instance of either a naturally refractory animal, or of an artificially specifically immunized one, which is proof against the introduction of a sufficient amount of a sufficiently virulent material.

We may distinguish three classes of individuals for present purposes:

* Read at a meeting held May, 1900.

1. Those who have recently had attacks and are considered recovered; here, in so far as their recovery is due to specific reaction against the cause, their recovery or resistance to continuance of the malady is of a specific nature.

2. Those who have had attacks at more remote periods, but who have retained sufficient specific antagonism to resist illness when exposed to possible infection; here the mechanism is specific.

3. Those who have never suffered from an attack, so far as can be ascertained. Of these subdivisions must be made: (a) those who have entirely escaped the influence of the infecting agent, non-specific; (b) those who have passed through unrecognised or unrecognisable attacks, specific; and (c) those to whom some specific immunity has been transmitted (not truly inherited from) by the mother, who herself may belong to either of the classes given.

Individuals (both man and lower animals) may be carriers of the given infecting agent, to whichever of the classes they may belong.

In respect to Class 1, it must not be assumed that when an individual has apparently recovered he has necessarily ceased to harbour the infective agent. Infective agents will be of greater importance if they are carried on the surface, or passed in excretions, than if they are confined to latent foci within his system. In the case of *diphtheria*, it is well known that *B. diphtheriae* may persist about the upper air-passages for months after apparent recovery from all illness. In *enteric fever* cases, the *B. typhi abdominalis* may persist in the urine for considerable periods (Petruschky, Horton Smith). In *plague*, cases have been described where *B. pestis* continued in the sputum thirty to forty-eight days after the complete cessation of fever, and when the diphtheria patients were apparently well (Gottschlich). The bacilli thus found were proved to be fully virulent for guinea-pigs.

It will probably be admitted that in such cases an individual, though apparently well restored to health, may really be a danger to his fellows.

As an instance of refractory animals retaining infecting agents, some experiments with the *Micrococcus melitensis* may be cited. Guinea-pigs are comparatively refractory to this organism; of a number of these animals which were infected, some died at considerable periods after the injection; the longest survivals were seventy-four and ninety-four days; in both of these the presence of the coccus was determined in certain of the organs as well as in the urine. Other animals which survived four, six, eight, and ten months were killed, and cultures were made to see whether the coccus was still present. In all of the cases the coccus was found, generally abundantly, in the urine.

(a) Killed after four months' growth only from kidney and urine.

(b) Killed after six months, large piece of spleen and loopful of urine both gave growth; other organs *nil*.

(c) Killed after eight months' growth from local caseous nodule, kidney (large piece), spleen (loop), femoral marrow (all from one femur), and urine (one drop).

(d) Killed after ten months' growth from two drops urine; organs (both large pieces and single loops remained sterile).

These observations are not without interest in showing with what tenacity an organism may remain in the urine of an animal* and be diffused by it. (It may be noted that no case of "laboratory infection" occurred during the course of these observations.) From this we

* Birt and Lamb failed to find the micrococcus in the urine of the human cases examined by them.

may pass to diphtheria. It has been found by a number of observers that the blood-serum of some untreated horses ("normal") possessed a more or less considerable quantity of a substance which had the power of neutralizing diphtheria toxin; the most carefully worked out cases are those of Dr. Cobbett, who showed that the relations of the neutralizing substance with different *diphtheria filtrates* agreed with those possessed by proper antitoxin of diphtheria; and that, so far as present methods go, there was no doubt that the substance in question was truly diphtheria antitoxin. At the same time it must be stated that a very considerable number of horses have been tested, and shown to possess no appreciable neutralizing power whatever in their serum. The presence of the antitoxin is, therefore, no normal condition of the horse, and the inference is that it is an acquired character. It may be doubted whether such a character can be acquired without the presence and action of the diphtheria bacillus or its products. Horses, I believe, are not known to be affected with diphtheria as such; but it does not follow that they may not harbour the bacillus at times in such a way as to engender the production of true antitoxin.

Whatever interpretation may be placed upon these data, the possibility of the horse acting as a disseminator of diphtheria cannot be entirely excluded.

From these considerations we are led to deal with the presence of apparently virulent diphtheria bacilli in the throats of persons who are not suffering from manifest illness, and the presence of neutralizing power of the blood-serum (for diphtheria toxin) of persons who are not known to have had diphtheria.

Many observers have recorded instances where diphtheria bacilli have been demonstrated in the throats of persons not suffering from the malady; several of these were, more or less, in attendance upon diphtheria patients. The serum of persons who had not suffered from diphtheria has been examined by a number of observers. Wassermann found that of the sera taken from thirty-four adults, as many as twenty-eight showed definite power of neutralizing diphtheria toxin; in most of the cases 1 c.c. of the serum was able to neutralize ten fatal doses when given in mixture; in the remaining cases no neutralizing power could be found. He also examined seventeen children of one and a half to eleven years of age; four of these had no neutralizing power, and in two there was delay in the time of death of the guinea-pigs, when, as before, ten fatal doses were given with the serum; the remaining eleven showed strong neutralizing power. Fischl and Wünschheim also found neutralizing power in sixty-eight out of eighty-two samples of serum obtained through the umbilical cord from placenta (i.e., blood of the child); in some instances 1 c.c. was able to neutralize twenty fatal doses of diphtheria toxin.

Perhaps the most interesting investigation of this sort is that of Loos, who examined the blood-serum of a number of children. One of these was tested, and found to have little or no neutralizing power; later, it became affected with diphtheria, and was again examined on two occasions—fifteen and sixty days after the illness. In both of these samples antitoxic action was found—more markedly, however, at the second examination. Two other cases failed to show action during the course of diphtheria; but examination after recovery showed that they, too, had acquired it. Lastly, in two children who were healthy, but in whose throats virulent cultures of diphtheria bacilli were obtained, strong antitoxic property was discovered in the serum. Such modes of inquiry are worthy of further study, especially in cases where healthy

individuals are found to be harbouring true diphtheria bacilli. In the children's portion of the Charité Hospital in Berlin there had been frequent outbreaks of diphtheria; it was consequently decided to make routine prophylactic injections (200 immunization units every three weeks). During a period of five months (Slawyk) observations were made upon 100 children. In twenty-four instances diphtheria bacilli were found in the throat without any symptoms accompanying their presence; in four cases diphtheria occurred. In respect to these, it is stated that, for certain reasons, prophylactic injections had not been properly carried out. It is not possible to be certain whether the twenty-four children, or some of them, would have escaped illness notwithstanding the bacilli, if the serum had not been given; moreover, their serum was not tested for neutralizing properties. Still, it is not impossible that the occurrence of the malady in the wards may have sometimes been spread from such individuals amongst whom the presence of diphtheria bacilli had not been suspected. When an individual has a considerable degree of natural resistance (as in the case of the rat), or acquired immunity, either passive by serum or active by absorption of bacillary products, it certainly is an advantage to the individual; but, in so far as he may unsuspectingly carry about virulent diphtheria bacilli, his peculiarity may be disadvantageous for his fellows.

Recently I have paid some attention to the dysentery which occurs in lunatic asylums, and which does not appear to differ materially in its nature from the dysentery of other countries. It appears probable that the disease is transferred from one individual to another, by some more or less direct means. Besides the cases which are recognisably dysenteric, one finds that a good many cases of intermittent or protracted diarrhoea occur. Occasionally opportunity is afforded of examining the condition of the colon in such cases, and in several instances it has been found riddled with ulcers of a nature resembling those seen in the less highly acute dysenteric cases. It is probable that these cases of diarrhoea form links which assist in keeping the disease endemic, especially as they do not give any apparent reason for care in the disposal of things which may have been infected.

It is, of course, impracticable to deal with every member of a community, and it would be especially difficult in the case of those who do not suffer during an epidemic. But it should be remembered that it may not be the severe cases and the slight cases only which contribute to the origin and spread of a disease. It is possible that the causative agents may be carried by individuals who, by reason of natural insusceptibility or by reason of an acquired specific immunity, may show no signs that they are doing so. It may, therefore, sometimes be of value to search for objective signs (specific organisms) amongst such apparently unpromising material. As a modification of an old commonplace saying, "Whatever you do with the pounds, pay some attention to the pence."

NOTIFICATION OF MEASLES.—The Newquay Urban District Council have resolved to ask the Local Government Board to consent to the removal of measles from the list of diseases to be notified. The resolution was arrived at in spite of the recommendation of the medical officer of health, and arose from the fact that an expenditure of £20 had been incurred in consequence of an epidemic which prevailed there during the early part of this year. Two members of the Council expressed the opinion that the notification of the disease had saved the town from an epidemic last year.