during work remains less during the repose which follows this work and during the sleep which succeeds this day of muscular activity."

But if we admit the presence of toxins in the periodic cases of these diseases—asthma, urticaria, epilepsy, "black strangury"—we must go further, and say that such toxins are probably an essential factor in all cases of these diseases. Periodicity is less marked in other cases, because the variations in the predisposing conditions are less regular or more complex; hygienic errors may be less marked, yet active. If this be so, the endogenous formation of toxins is of interest in view of recent theories as to immunity against microbes. In autointoxication certain organs or tissues deal with certain foods imperfectly; in immunity the production of cytotoxins, haemolysins, etc., is regarded as resulting from an alteration of the normal food-assimilating powers of the tissues. Whether the toxins originate directly in the intestine or in the muscles future investigation must show. In favour of the latter view are two points:

1. The diseased condition of the muscles in "black strangury" of horses.
2. A markedly predisposing condition is defective muscular exercise.

It is to be noted that this deficient use of voluntary muscle is accompanied by perverted contraction of involuntary muscle in asthma, urticaria, and possibly epilepsy. In asthma there is spasm of the smaller bronchial tubes, and probably of the arterioles; in urticaria, spasm of the arterioles. (N.B.—Urticaria and asthma are often concurrent or intercurrent.)

In epilepsy there is, of course, spasm of the voluntary muscles; but the idea of sudden cerebral anaemia in epilepsy is one that dies hard, and will take a good deal of dislodging from the mind of any one who has observed, as I have several times, the initial groan and epileptiform movements which sometimes accompany simple syncope. For example, these symptoms occurred in an attack of syncope brought on in an asthmatic man, aged 54, by slight intranasal interference; and again in a cabdriver, aged 26, while having an abscess opened. In neither case has there been any question of epilepsy before or since. And I have to suggest that just as the poison causes spasm of the involuntary muscles of tubes or vessels in asthma and urticaria, so it may in those of the cerebral vessels in epilepsy. This would not preclude it acting on the cerebral cortex directly, or, indeed, on the nervous system generally, both in epilepsy and asthma. The cumulative effect of such toxin acting over a period of time might not only result in an epileptic fit, but might also do much toward inducing the excitable condition of the cortex which is supposed to exist in epilepsy, or the condition of the central nervous system which Dr. Sidney Martin⁵ thinks exists in asthma, "a condition which cannot be defined categorically, but only expressed vaguely as that which is present in the individual predisposed to asthma."

In the "Monday-morning disease" of horses the poison, as might be expected in animals with such muscular power and exercise suddenly immured and overfed for thirty-six hours in dark stables, is much more powerful than those in the human being, and often is fatal. But it may well be of kindred nature; here also the blood vessels seem to be attacked. The difference between the stimulating effect of the poisons in the human diseases and the paralytic effect in that of horses suggests comparison with stimulating and paralyzing doses of alcohol and other drugs. While haemolysis is pronounced in the horses, it is to be remembered that blood extravasations are frequent in the human diseases. I have records of several cases of petechiae and blood-stained sputum in asthma; haemorrhagic varieties of erythema are well known, and the last case of epilepsy I saw showed, twenty-four hours after the fit, a diffuse venous duskiness of the skin of the forehead as if from capillary extravasation. This, however, might be fairly regarded as asphyxial.

While such toxins are an efficient cause of the diseases mentioned, in no case can they be a sufficient cause; there must be other factors. These must also demand treatment, but the importance of preventing toxin formation by suitable hygiene and of procuring rapid elimination of such when formed is obvious. For example, in asthma, after intranasal treatment, a teacher took fortnightly doses of blue pill and salines, and has been able to work for the last four years, though previously off work seven years. I think I have also seen benefit in epilepsy from a weekly blue pill, but of this I cannot be sure.

As a final proof of the position here stated, I should like to

mention one undoubted case of toxic disease (toxic amblyopia) which is remarkable because it was induced by the same conditions as in "week-end" asthma, because it was pronounced in its effect, and because it was cured by proper open-air exercise.

CASE IV.—A teacher, aged 24, who took little exercise, and spent most of his spare time in study, consulted me in July, 1899. Vision: left barely counts fingers; right, 3; no marked fundal change. Dr. Maitland Ramsay, of Glasgow, to whom I sent the case, and to whom is due the credit of the cure, emphasizing the fact that the defect in the visual field was central, not peripheral, and that there was persistent oxaluria, gave a hopeful prognosis. The patient was at first made to rest in bed in a dark room, and got pilocarpin injections and other eliminants. Later he was allowed to get out with dark protection glasses, and medicinal treatment (hyd. perchlor., ammon. chlor., pot. iod.) was continued. During the winter vision became worse, so that he could not see the chairs in my consulting room, and stumbled against them. About a year after I first saw him there was no improvement, and a well-known ophthalmologist in Edinburgh gave a very black prognosis, and said patient would never be able to read again. Shortly after this, strychnine having been added to the medicine, the patient thought he began to notice slight improvement; he could just see the largest test types. Dr. Ramsay had pressed for a sea voyage. To this patient was reluctant, but in July, 1900, he went for a trip to Shetland. By the time he reached Kirkwall he could see the town clock. On his return a few weeks later distant vision was 2. A trip to Canada completed the cure, and he could read the smallest print.

Here the toxin hit the organ most strained, but while its effects were most manifest in the eyes they were doubtless widespread, as seems likely from the oxaluria. The importance of a sea voyage in quickening metabolism is obvious.

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CASE OF GENERAL PNEUMOCOCCAL INFECTION, WITH FEW SYMPTOMS.

By GEORGE PARKER, M.A., M.D. CANTAB.,
Physician to the General Hospital, Bristol.

This case seems worth recording, not because generalized pneumococcal infection is at all rare, but because it shows how few of the recognized symptoms may be present in children, even in fatal cases. Here was a child whose blood and pericardial fluid gave a pure culture of the pneumococcus, who had peritoneal and pulmonary lesions, and whose mediastinum and pleurae were obstructed with effused lymph. His illness, too, had probably lasted six months, and yet for the last month, when under my care, there were hardly any symptoms of acute illness except a few rales and dullness at the base of one lung, and at times a slight rise of temperature, which was entirely normal for the last nine days of life.

History.—G. B., a male child of 17 months, was admitted into the Bristol General Hospital on January 21st, 1903, with a history of broncho-pneumonia, which had been recognized for a fortnight. He had been breast-fed, and was always healthy till August, 1902, when he suffered from measles, followed by an attack of diarrhoea. For the next two or three months he was feverish and ailing, but there was no cough. The mother remarked that during that time he was ravenous, and seemed to be always hungry.

State on Admission.—His temperature was normal; the bowels were regular, and there was a faint trace of albumen in the urine. In both lungs there were a few scattered rales, most numerous at the right base, where there was some dullness on percussion and diminished respiratory murmurs. There was little or no cough. Two days later the temperature rose to 101°, but fell to normal in two days, and afterwards showed only smaller oscillations before it became permanently normal. The lungs cleared up, and frequent examinations failed to show anything except slight dullness and a few rales at the right base. The abdomen, the heart, and the other organs were normal, and the patient slept and took liquid food well. However, at times the breathing was very rapid—50 to 60 per minute—the skin was remarkably white and pallid, though the palpebral conjunctivae were not blanched, and there was also very slight oedema of the legs. As there seemed little or no evidence of kidney disease or heart failure to account for this, the blood was examined carefully. The red cells were nearly 5,000,000, while the white numbered 54,500. The differential count made by Mr. F. Leighton, the clerk, gave polymorphous cells 61 per cent., eosinophile 1.6 per cent., small lymphocytes 31.6 per cent., large hyaline 4.6 per cent., neutrophile myelocytes 0.6 per cent., eosin ditto 0.2 per cent., and basophiles 0.2. The haemoglobin was 50 per cent. and a few nucleated red cells were present. There was no enlargement of the liver, spleen, or other glands or evidence of any haemorrhage. The optic discs were normal. In order to avoid the possibility of overlooking any fluid in the pleura from the uncertainty of pulmonary signs in children, a needle was twice inserted into the right pleura, but with no result,

and the chest was examined by the x rays. Four weeks after admission the patient died rather suddenly with practically no symptoms except the occasional quick breathing, the pallor, and the abnormal blood count. Shortly before his death another differential count was made with the following result: Red cells 4,310,000, polynuclear 46 per cent., eosin 1.2 per cent., small lymphocytes 45 per cent., large hyaline 4.8 per cent., neutral myelocytes, 2.2 per cent., eosin ditto 0.8 per cent., total leucocytes 73,600.

Necropsy.—The necropsy was carried out by Dr. Newman Neild, to whom I am indebted for the following notes. The body was considerably wasted and anaemic. There was slight oedema of the hands and well-marked oedema of the legs and feet. A growth of fine hair appeared over the whole skin, most marked about the shoulders. The tonsils were normal, the larynx, trachea, and large bronchi were slightly injected. On opening the thorax the anterior mediastinum was found to be full of organizing lymph still somewhat gelatinous. Over the lower lobe of the right lung were thickly distributed masses of soft green lymph. In some places over the lower lobe there were adhesions to the chest wall. On section the whole of the middle and lower lobes showed signs of broncho-pneumonia apparently progressing towards recovery. The upper lobe showed a similar affection to a much less extent. In the left lung the lower lobe showed also broncho-pneumonia in the resolving stage, especially at the base. Thick flakes of green lymph were entangled among the large vessels at the base of the heart. The blood in the heart was fluid, but a large straw-coloured clot was lying in the right ventricle. The valves and the heart muscle were normal to the naked eye. The pericardium contained about half an ounce of greenish serum with flakes of lymph. The right auricle was somewhat dilated. The stomach, oesophagus, and intestines were normal. The lymphatic glands at the angle of the jaw were enlarged, those elsewhere were normal. There was very slight injection of the peritoneum, and a few flakes of lymph were found in the peritoneal cavity. The kidneys were congested, but otherwise normal. The urine showed a cloud of phosphates. The spleen was firm and not enlarged. The Malpighian bodies were translucent and enlarged. The marrow in the ribs was macroscopically normal, that in the femur was rather paler than usual. Cultures taken with due precautions from the pericardium and the heart blood gave a pure growth of the pneumococcus.

Pneumococcal septicaemia is, of course, a common occurrence. In pneumonia, especially if we examine the most severe cases and take the blood shortly before death, it is very frequent, and even in the course of ordinary attacks it can sometimes be found. Prochaska, the latest observer I have noted, found it in 38 out of 40 consecutive cases. It is found, too, in other diseases due to the pneumococcus, such as arthritis, tonsillitis, otitis, empyema, and peritonitis. Foulerton and Dieulafoy found it in their remarkable cases of phlegmonous gastritis, and G. Blumer notes that a general infection of the blood is often present, not only in pneumonia but also in simple oedema and congestion of the lungs. The difficulty raised by Durck's discovery of the pneumococcus in the lungs of some healthy individuals need not trouble us here, for there were ample evidences of its pathogenic virulence in the various organs and cavities. It does not seem certain where the primary entrance of the infection took place.

The lesions outside the lungs are at least as marked as those within them. The broncho-pneumonia may have been a late complication of the original trouble. Some 75 per cent. of the cases of empyema in children are pneumococcal, and Foulerton has shown reason for thinking that many of these are primary and without any lung affection. Indeed, Washbourn proved that the pneumococcus can pass through the healthy lung without injuring it and set up lesions elsewhere. In peritonitis, too, there may be no lung affection, and the disease may simulate typhoid or appendicitis, and commence with an attack of diarrhoea.

A recent case under my care was admitted as appendicitis, and was found to have a large amount of pus free in the peritoneum, which gave a pure culture of the pneumococcus. In this patient, as in G. B., I was struck with the very slight effect on the general activity of the patient which the infection produced, though marked pyrexia existed in the former case and a nearly normal temperature in the latter.

A high temperature is, of course, the rule in adults and older children. Nuthall and Billington,¹ in reporting 13 cases of pneumococcal infection, refer to its markedly remittent character and the "typhoid state," which marks the later stages of the disease. Newton Pitt, however, in a recent discussion, pointed out that with infantile empyema the temperature may be normal throughout the whole course of the disease in certain cases. It is not clear what is the cause of this apyrexia, but it is not likely that the degree of virulence of the special coccus has anything to do with it. If we suppose that in the present patient the acute attack was over before admission, still a month is a long while for

the pneumococcus to remain in the blood and lymph with little or no pyrexia.

The blood counts do not seem on the whole to disagree with the *post-mortem* findings, though I was disposed at first to regard the marked lymphocytosis with apyrexia as due to some form of leukaemia. In the pneumonia of adults a marked leucocytosis occurs in all but the most severe or the very mildest cases, as is well known, and is due to an increase of the polynuclear cells, which amount to 80 or 90 per cent., while the lymphocytes are reduced to 4, or even 2 per cent. However, in children under 1 year all this is changed. A leucocytosis is made up chiefly by an increase of lymphocytes, except perhaps in severe intestinal disturbances, when the adult type is seen. Even in healthy children of this age, the statistics of Alf. Japha, of Berlin, show that the small lymphocytes are normally 54 per cent. and the large ones 4, while the polynuclear are only 42 per cent. Thus our count of 73,600 white cells made up of 49 per cent. lymphocytes and 46 polynuclear ones is not out of the way, and Cabot somewhere records a case of pneumonia in a child where the white cells amounted to 94,600 and lymphocytes to 66 per cent. Even the slight excess of large lymphocytes is a common feature in childhood, though it occurs also after the defervescence of pneumonia in adults, where Tarck has found them numbering 16 per cent. The eosinophile myelocytes have been looked upon as peculiar to leukaemia, but of late have been found in pneumonia also. On the whole, the blood counts, remarkable as they were, did not aid us much, and unless a culture had been made from the blood during life it is hard to see how the condition could have been determined. Possibly the iodine reaction which has been recently used in pneumonia might have given some indication.

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NOTE ON THE ABSENCE OF B. COLI, ETC., FROM THE NORMAL OYSTER.

By R. TANNER HEWLETT, M.D., M.R.C.P., D.P.H.,

Professor of General Pathology and Bacteriology in King's College, London.

UNLESS it can be shown that the bacillus coli and allied forms, and the bacillus enteritidis sporogenes are not present in shellfish living in uncontaminated waters, the bacteriologic examination of shellfish for evidence of sewage pollution can be of little value, since it is based upon the search for, and detection of, these species of bacteria. The researches of Professor Boyce and of Dr. Klein, however, seem to have proved that, contrary to what obtains in the higher vertebrates, these microbes are normally absent both from the exterior and from the digestive tract of the principal edible molluscs, and make their appearance only as a result of sewage pollution.

I am able to confirm Dr. Klein's observations, and have no doubt that the presence of organisms of the colon or enteritidis (Gaertner) group is indicative of sewage pollution, and that the presence of the bacillus enteritidis sporogenes is further confirmatory evidence of this.¹

I have recently examined some 32 oysters from various sources (the majority from the Roach River, a few "Mumbles," "Portuguese," and "Anglo-French"), and with the exception of two—a Portuguese and a Mumbles—not one contained any of the above-named organisms. The method of examination was to scrub the shells in clean water, dry them, and then to open with sterile instruments. The oyster was next cut up with sterile scissors, and two to four drops of the milky fluid were sown into (a) two Durham's fermentation tubes, containing litmus, glucose, bile-salt peptone water (McConkey); (b) one Parietti broth tube (0.2 c.cm. Parietti); (c) two milk tubes, which were heated and incubated anaerobically; (d) one surface carbol-gelatin plate. The tube cultures and plates were incubated and examined, and subcultures from suspicious tubes and colonies were made and examined. In a few instances carbol-gelatin plates and bile-salt tubes were inoculated from the contents of the digestive tract alone.

From my observations I have no hesitation, therefore, in concluding that oysters from waters uncontaminated with sewage do not normally contain the colon or allied bacilli or the bacillus enteritidis sporogenes.

¹ *BRITISH MEDICAL JOURNAL*, February 21st, 1903, p. 417.