

suggestion is only one step farther than this and renders the explanation of the case less difficult. I would suggest that the transient speech defects in these two cases were of the same nature as are the speech defects sometimes seen in cases of left hemiplegia in right-handed persons.

The incompleteness of the notes upon speech defect in this case is due to the fact that it did not present itself as a case of aphasia. The handwriting was tested, as it is a routine practice in the National Hospital for the Paralysed and Epileptic for each patient to write his name in the notes. Word vision was tested in the routine examination of eyes presenting optic neuritis.

A PRELIMINARY NOTE UPON CERTAIN ORGANISMS ISOLATED FROM CANCER AND THEIR PATHOGENIC EFFECTS UPON ANIMALS.¹

BY H. G. PLIMMER, M.R.C.S. ENG., F.L.S.,

PATHOLOGIST AND LECTURER ON PATHOLOGY AND BACTERIOLOGY,
ST. MARY'S HOSPITAL.

DURING the past six years I have been studying the cell-inclusions which are found in cancer and their relation both to the origin and course of the disease, and for this work I have had to examine 1278 cancers taken from various organs and parts and of all possible varieties. Out of this large number of cases there have been a few—nine in all—in which the cell-inclusions have been extremely numerous, so that at the growing edge, and even far into the tumour, scarcely a cell could be found without an inclusion, sometimes with as many as 36 even of these inclusions in one cell, and these bodies have been similar to those which Metchnikoff, Ruffer, and others, as well as myself, have regarded and described as parasites standing in causal relationship to the disease. In two out of the nine cases mentioned these bodies have been present in enormous numbers, and I have succeeded in isolating from the last of these remarkable cases an organism which is pathogenic in a peculiar manner to certain animals and whose virulence I have been able to keep unimpaired for some months.

PREVIOUS WORK ON THE EXPERIMENTAL PRODUCTION OF TUMOURS IN ANIMALS.

The only work, I think, that needs mention here in connexion with this heading is that of Sanfelice in Cagliari and of Roncali in Rome. Sanfelice has produced tumours in animals with organisms which he isolated from infusions of various fruits, and they both have isolated organisms from cancers, which I believe from their descriptions—I have not seen their cultures—are morphologically somewhat similar to those I am about to bring before you. But Sanfelice's organism appears to have been very difficult to isolate in a virulent form from human cancer and to keep virulent, so that in his last paper² he treats only of the organisms derived from fruit infusions and of their effects upon animals. Most of the statements are doubted by the German pathologists, including such a good observer as Baumgarten, but from my own experience I do not find any reason to doubt any of Sanfelice's statements, and I think that he deserves the greatest credit for removing the study of the etiology of cancer from the histological to the experimental region of work.

ON THE METHOD OF ISOLATION ADOPTED.

The cancer from which the organisms I am about to describe were isolated and with which my experiments have been made was taken from the breast of a woman, aged 35 years; it had a history of only two months' duration and it was growing rapidly at the time of the operation. Immediately after removal I examined a fresh scraping and finding such an extraordinary number of the bodies I have mentioned in the cells I cut, with all possible precautions against contamination, with a carefully sterilised knife, very thin slices from the growth which I placed with a little of the juice scraped from the cut surface in a flask containing the following liquid, which was of course carefully sterilised.

This medium consisted of an infusion made from cancer, just as the ordinary beef infusion is made, to which was added, after careful neutralisation, 2 per cent. of glucose and 1 per cent. of tartaric acid. This medium was the outcome of many trials with all kinds of mixtures and I tried it in this case as I had already got similar organisms to grow in it from two previous cases but they had no pathogenic properties, and this, I think, was due to the omission of the next step. This medium, too, is particularly useful, as hardly any bacteria, however hardy, will grow upon it. Then, remembering that in the body these organisms were under anaerobic conditions, I exhausted the air from my flasks and passed hydrogen into them and finally sealed them up. This I have found is of great importance as regards the maintenance of the virulence, and I find consequently that there is no falling off in the virulence of my cultures which are as active now as they were four months ago. Five flasks were made in this way, but in spite of precautions two became contaminated with moulds; in the other three, however, I got after from three to five days a pure culture of the organism described below has been kept growing in this and various other media ever since.

MORPHOLOGY AND RELATION TO MEDIA.

The organism is apparently a saccharomyces, but I am informed that, according to some authorities, such as De Bary, Cuboni, and Duclaux, the saccharomyces are nothing but the developmental stages of fungi which really belong to either the phycomycetes, the ascomycetes, or the basidiomycetes. Moreover, they state that in some species of mycelium-forming fungi, single parts, especially conidia, can grow in the saccharomyces form on certain nutrient media, so I will not attempt to locate this organism at present. Sanfelice and Roncali, however, definitely state that the organisms they have isolated are blastomycetes.

When grown in the medium described these organisms produce a cloudiness which becomes visible in about 48 hours and increases till about the sixth day, when the growth sinks to the bottom, the medium then becoming clear; no scum or pellicle is formed. When grown on this medium solidified with agar the organisms form small round colonies which remain separate. After some weeks the colour, which was originally white, becomes yellow. The colonies do not attain at any time a great size.³ Gelatin is not liquefied, but the growth on this medium is never luxuriant. On potato a thick white layer is formed which in about two weeks will cover the entire surface, changing then to a yellowish-brown colour. They will grow aerobically, but not so well, at any rate at first, and they lose their virulence in a short time if continuously grown in this way. Microscopically they are round bodies, frequently growing in clumps, with a central portion which stains deeply, and in most cases with a thin, strongly refractile capsule which sometimes shows a double contour; but some young forms can be seen which are apparently without a capsule. The size varies from 0.004 millimetre to 0.04 millimetre. Their reproduction appears to be by budding, but I have fancied that I have also seen in a few instances endogenous budding; of this, however, I am not certain. These bodies correspond morphologically with those found in the original tumour and also with those described by Ruffer and myself and by some others of those who have worked at the microscopical appearances of cancer.

EXPERIMENTAL RESULTS.

I have selected from the experimental work which I have done with these organisms those experiments which seemed to me to be the most important. Up to the present time I have not been able to make any such experiments upon such animals as would allow of the easy bringing of these organisms into contact with a likely epithelial surface with the exception of the cornea (*vide* Experiment No. 4), but through the kindness of Dr. Rose Bradford I have been enabled now, at the Brown Institution, to inoculate a bitch in the mammae, but the time is as yet too short to enable me to make any statement as to the result. The cultures used in the following experiments were made in the medium previously described.

1. *Rabbit*.—Intravenous injection of five cubic centimetres of an eight days old culture. There was no obvious result.

³ The following specimens were shown: (1) sections of the cancer from which the cultures were made; (2) the cultures on various media; (3) preparations of the cultures; (4) sections of the organs of the animals in which tumours had been produced; and (5) animals, or portions of them, in which tumours had been produced.

¹ A paper read before the Royal Society on March 9th, 1899; communicated by Professor J. Rose Bradford, F.R.S.

² *Zeitschrift für Hygiene*, 189

The rabbit was killed 13 weeks afterwards and was found to be apparently normal.

2. *Rabbit*.—Intraperitoneal injection of 10 cubic centimetres of a 21 days old culture. There was no obvious result. The rabbit was killed eight weeks afterwards and was found to be apparently normal.

3. *Rabbit*.—Subcutaneous injection of five cubic centimetres of a three days old culture. There was no obvious result. This rabbit was used later for Experiment No. 4, and when killed 14 weeks after Experiment No. 3 it was found to be normal; nothing was found at the seat of injection.

4. *Rabbit*.—Both corneæ were scraped and the sediment of a 10 days old culture rubbed over them. The rabbit was killed in 48 hours. There was considerable proliferation of the corneal epithelium which had forced its way into the subjacent tissue. The organisms were found in the epithelial cells after fixing and staining, with appearances similar to those of the inclusions in cancer cells as described by Ruffer and myself.

5. *Rabbit*.—Trepined and inoculated beneath the dura mater with five cubic centimetres of a seven days old culture. The rabbit died in nine and a half days; the wound had healed. The brain and cord contained the organisms in large numbers. Pure cultures were obtained from the brain, the liver, and the kidney. Nothing was obtained from the blood, the spleen, or the peritoneal fluid.

6. *Rabbit*.—Trepined and inoculated beneath the dura mater with five cubic centimetres of a three days old culture made from the brain of No. 5. The rabbit died in eight days; the wound had healed. Organisms were found in the heart, the blood, the brain, and the cord. Pure cultures were made from the brain, the cord, the kidney, and the liver.

7. *Guinea-pig*.—Subcutaneous injection of five cubic centimetres of a 10 days old culture. There was no obvious result. The guinea-pig was killed in 15 days and was found to be apparently normal; nothing was found at the seat of injection.

8. *Guinea-pig*.—Intraperitoneal injection of 10 cubic centimetres of a three weeks old culture. The guinea-pig died in 20 days. The liver, the lungs, and the peritoneum were studded with new growths of a white colour; the lymphatic glands in the abdomen were enlarged. Pure cultures were made from the liver, the lungs, and the abdominal glands; nothing was obtained from the blood. Sections of the above-mentioned parts showed new growths of an endothelial nature, with the organisms within the cells and free in the tissues.

9. *Guinea-pig*.—Intraperitoneal injection of 10 cubic centimetres of an eight days old culture, made from the abdominal glands of No. 8. The guinea-pig died in 17½ days and showed the same appearances as No. 8. Cultures were made as before and also from the blood. In this case the omentum was also studded with new growths.

I have given here some of the failures and successes which have been constant, and I should like to add that Professor Wright of Netley has repeated some of the experiments I have made and that his results coincide with mine.

The important point, of course, of all this is—the experimental production of malignant tumours in animals by an organism isolated from a malignant tumour in man. That these experimental tumours are, so far with one exception of endothelial origin is due to the fact that until I was enabled to inoculate a dog I found it very difficult to get the organism in contact with likely epithelium; all the above methods of inoculation, save one, could only bring them into contact with endothelial surfaces. No. 4 (the corneal experiment) is the only one in which an epithelial surface was tried and in this case the great proliferation of the epithelium, the appearances of the organisms in the cells, and the irritation produced, were very striking. But the fact of being able to excite a malignant growth with an organism isolated from cancer is, I think, a point of some importance in the etiology of cancer. I am at present experimenting with the view of observing the effects produced by these organisms when brought into contact with epithelia.

The deductions which I think may fairly be made from these observations and experiments are as follows:—

1. That there are certain cancers which occur very rarely in which there are in enormous numbers intracellular bodies of the kind described by Ruffer, by myself, and by others as parasitic protozoa. (From the rarity of these cases and their

comparatively acute course one is tempted to think that they are not due to the same cause as ordinary cancers, but there is really no more difference between them and ordinary cancers than between acute and chronic tubercle.)

2. That by the use of appropriate means these intracellular bodies can be isolated and cultivated outside the body.

3. That these cultures when introduced into certain animals can cause death with the production of tumours, so far with one exception of endothelial origin, and that pure cultures can be made from these growths which when inoculated into suitable animals will produce similar tumours.

St. John's Wood-road, N.W.

A CASE OF TUBAL GESTATION WITH RUPTURE AND FATAL HÆMORRHAGE AT A VERY EARLY PERIOD OF PREGNANCY.

BY F. LUCAS BENHAM, M.D., M.R.C.P. LOND.

THE following case I believe to be sufficiently uncommon to be worthy of record.

The patient was a woman, aged 23 years, who had been married for three and a half months and had never borne a child. She was said to have formerly drunk somewhat to excess and latterly she had suffered from indigestion. Otherwise her health and habits had been generally good. Menstruation had always been regular. Since her marriage (at the end of April, 1898) she had missed two periods—May and June. The July period was profuse, lasted for three weeks, and was followed after an interval of one week by the next period (early in August) which appeared to be normal and which ceased on August 12th, two days before the present illness. On August 14th, 1898, I was asked to see the patient in the temporary absence of Dr. C. A. Crane (who had not previously seen her, however). She was said to be suffering from abdominal pain. I visited her at about 2 P.M. and found her lying in bed. She said that she had not felt well that morning and that on trying to get up she did not feel able to do so. At 10 A.M. severe abdominal pain came on. She admitted having eaten some pork sausages and ice-cream the day before. There was no nausea, vomiting, or diarrhoea. The bowels had been last moved naturally on the previous morning and were regular. The tongue was clean and moist. The skin was very pale and distinctly cool, but the patient had naturally a white or somewhat sallow complexion associated with black hair, so that she had often been supposed by strangers to be Italian. There was, however, no marked pallor of the lips. The pulse was weak and compressible. She was perfectly conscious, not collapsed, could move about readily in bed, and did not seem dangerously ill. I examined the abdomen carefully. There was no distension or abnormal note on percussion and the knees were not drawn up. There was diffused pain over the abdomen, especially over the lower part, and it seemed somewhat greater on the right side than elsewhere; there was slight general tenderness. No tumour was to be felt. The patient confidently denied pregnancy. No vaginal examination was made. The treatment ordered was half an ounce of castor oil to be taken at once, to be followed by one or two draughts containing opium and belladonna. Hot fomentations were to be applied to the abdomen and milk and soda water or arrowroot were to be taken as food. At about 11 P.M. the patient's husband called to tell me that his wife was no better, that the pain was very great, and that she wanted relief and sleep. Two doses of castor oil had been given without any action of the bowels. I went again to the house and found the patient very much worse—in fact, dying. She was extremely pale, with pinched face and staring eyes, and she was gasping for breath. She complained of pain all over the chest and abdomen, that her head was light and swimming, and that she could not get her breath. The skin was cold, except over the abdomen where fomentations had been applied. The abdomen was much distended and dull in the flanks. The patient had passed no urine and had been slightly sick at times. The heart could be felt beating and was rapid, the respiration also was hurried, and the radial pulse was imperceptible. I saw that she could only live half an hour and that it was too