MICROSCOPICAL AND EXPERIMENTAL OBSERVATIONS.

By Dr. BUCHANAN.

Non-motile spirochaetal forms were found in the urine of the patient on examination by dark-ground illumination. The closely set, elementary spirals typical of the genus *Leptospira* were not evident. This may have been due to the fact that the forms seen were lying on or under epithelial cells which obscured their delicate structure. In stained films of urine a few spirochaetes were found, some of which showed one end or both with small hooks, which are a feature of *Leptospira icterohaemorrhagiae*.

Intraperitoneal inoculation of the urine into a guinea-pig proved fatal in fourteen days. The ears, nose, conjunctivae, and feet were visibly jaundiced. The subcutaneous tissue showed deep jaundice along with innumerable petechial haemorrhages. There were large subpleural haemorrhages in both lungs, presenting a typical "butterfly" appearance. The liver and spleen were enlarged, but the marked congestion masked any evidence of jaundice in the liver. The kidneys showed intense congestion, and numerous subcapsular haemorrhages were prominent. The suprarenals were enlarged and congested. The intestines showed adhesions and haemorrhages. Organisms identical with *Leptospira icterohaemorrhagiae* were found on dark-ground examination to be very numerous in the liver, but fewer in the other organs. They were also present, but less numerous, in the blood and urine. In sections of the liver stained by Levaditi's method leptospiral forms were abundant.

Another guinea-pig, inoculated with an emulsion made from the liver of the infected animal, died in five days with lesions similar to, but not so marked as, those described above.

Occurrence of Leptospira in the Rats of the Neighbourhood.

Three live wild rats were obtained by the courtesy of the pit owner, two from one of the coal mines and one from the surface at about a quarter of a mile from the pits. Motile and characteristic leptospiral forms were found by dark-ground examination in emulsions made from the kidneys of the surface rat and one of the pit rats. No spirochaetes were found in the other organs, the urine, or the blood. The blood was infected with *Trypanosoma lewisi*. The rats were well nourished and showed no signs of disease.

Guinea-pigs were inoculated intraperitoneally with kidney emulsion from each of the three rats. The one inoculated from the surface rat was found dead on the seventh day. It showed definite jaundice, haemorrhages, and lesions similar to those found in the animal inoculated with the patient's urine. Leptospiral forms were found as before. Noguchi's medium was inoculated from the liver and blood of this guinea-pig. After six days' incubation at 37° C., actively motile and obviously multiplying forms of leptospira were still demonstrable at that period.

A guinea-pig inoculated from one of the pit rats died thirteen days after the injection. Leptospiral forms were again found in the blood, urine, and organs generally. Jaundice and haemorrhages were a feature of the post-mortem examination. The remaining guinea-pig, inoculated from the second pit rat, in which no organisms were found, is still alive and apparently well up to date—that is, sixteen days after inoculation.

CONCLUSIONS.

It has been definitely established that the leptospiral organisms found in man and rats in the infected area produce lesions typical of infectious jaundice when inoculated into guinea-pigs. The result of the inoculations proved fatal in from seven to fourteen days. Subinoculation into the same species, with either human or rat strains from dead infected guinea-pigs, proved more rapidly fatal in both cases, the period being five to six days.

The two organisms isolated in this instance from man and wild rats are morphologically identical. The organism has been cultivated. Its characteristics in dark-ground illumination consist of very minute regular spirals throughout its entire length, and a hook at one or both ends. The

hooked end rotates in the manner of a propeller, and progress occurs in the direction of the unhooked end. If both ends rotate it remains practically in the one place.

The pathogenic action, morphology, and behaviour in culture of the leptospira show it to be, so far as the work has proceeded, identical with the Japanese, European, and American strains described and compared by Noguchi.

Further investigation is in progress, the results of which will be published in detail at a later date.

The microscopic and bacteriological part of the work has been carried out in the Pathological Department of the Royal Infirmary, and the experimental part in the Royal College of Physicians Laboratory, Edinburgh.

Press communications by the Scottish Board of Health have already appeared in the *Scotsman*. The information given resulted from the above bacteriological investigation.

METASTASIS OF MELANOTIC CANCER EIGHTEEN YEARS AFTER REMOVAL OF THE EYEBALL.

BY

A. E. WEBB-JOHNSON, C.B.E., D.S.O., M.B.,

F.R.C.S.,

SURGEON TO THE MIDDLESEX HOSPITAL;

AND

C. E. ALEXANDER MACLEOD, F.R.C.S.

THE following case is of some interest, and we feel should be put on record.

A lady, aged 57, came under our care in August, 1922, complaining of a swelling below the left scapula, which she had noticed for two weeks. She also complained of gradual loss of strength during the past few months. She had no pain at the site of the swelling, but some dull aching round the chest. An elastic swelling, oval in outline and about the size of an ordinary lemon, could be felt protruding from beneath the inferior angle of the scapula on the left side.

The patient gave a history of having had the left eyeball removed in June, 1904, by the late Mr. Juler. Mr. Frank Juler has kindly given us an extract from his father's notes on the case. The eyeball was removed for suspected sarcoma of the ciliary body. There was a large dark brown mass in the vitreous, just behind the lens, with haemorrhage upon it. There was some bulging of the periphery of the iris. Though there is no note of the histological appearance of the tumour, there can be little doubt that it was an intraocular melanotic cancer.

The swelling on the back was explored, and was found to be a dark pigmented growth involving the sixth and seventh ribs, near their angles. A mass, including about five inches of the length of each of these ribs, was removed. The growth was adherent to the underlying pleura, which could be felt to be adherent to the lung. There were some small dark nodules, forming prominences on the surface of the pleura. The patient recovered rapidly from the operation, and returned to her usual domestic activities.

The growth removed proved to be a melanotic cancer. An examination of the urine at the time of operation, and one month later, showed that there was no melanin or melanogen present. Three months afterwards the patient began to fail. In the middle of December, 1922, she complained of numbness and tingling in her right foot. This was followed in a few weeks by complete loss of power, with rigidity. Shortly afterwards the left hand and arm were affected in the same way, followed by the same condition in the left leg, and then in the right hand and arm. By the beginning of April, 1923, both arms and legs were paralysed and rigid. There was loss of control over the bladder, and obstinate constipation. The patient died on April 16th, 1923.

No general discussion of the delayed appearance of metastases from melanotic cancer of the eyeball is called for, as the whole subject has been dealt with recently by Mr. W. G. Spencer in his Bradshaw Lecture.¹ It is, however, worthy of note that so late as eighteen years after removal of the primary tumour there was still no evidence of metastasis in the liver, if, as stated by Garrod,² melanuria can be taken as an indication of that having occurred. In melanotic cancer of the eyeball death usually occurs within three years of operation, but numerous instances of delayed recurrence or metastasis have been reported. Cairns³ reported a case of metastasis in the scapula eighteen years after removal of the eyeball, and metastasis has been delayed as long as twenty-four years,

as in the case reported by Olbert,⁴ and referred to by Spencer. Lawford and Treacher Collins⁵ in 1891 discussed the subject of melanotic growths of the uveal tract, with notes of 103 cases. They were able to trace 79 of the patients, of whom 40 were dead; in 2 of these the interval between the operation and death was seven and eight years respectively. Of the 39 patients who were still alive, one had been operated on eighteen years and another sixteen years previously, while the intervals in the other cases ranged from seven months to nine and a half years. In spite of their analysis of the fatal cases, they ventured to say with regard to 20 patients who were still alive and well three or more years after the removal of the primary growth, that these cases might be considered with great probability, but not with certainty, as permanent cures. It is, however, obvious from a study of their own fatal cases, from the case we are reporting, and from numerous other instances, that no such probability can be assumed. Melanotic cancer of the eyeball differs from every other manifestation of cancer in the length of time for which metastasis may be delayed, and the prolonged intervals have led to the suggestion that it is not a true metastasis, but an origin *de novo*.

It is remarkable that these growths spread with great rapidity and lead to a fatal termination very quickly after a recurrence shows itself. This suggests that the new manifestation is due rather to a breakdown in the resistance of the individual than to a sudden activity of the disease; for actually or potentially the disease must have been present the whole time, and has presumably been kept in bounds by the resistance of the patient. If we are to make further progress in the treatment of cancer it would seem that, in addition to the eradication of its local manifestations, we must adopt some means of increasing the resistance of the individual to the disease. In no part of the body would it seem more feasible to remove the whole of the primary tumour than in cases of cancer of the eyeball, and yet we are faced with these delayed metastases.

It is early days yet to know what may be expected from the experiments on the production of immunity to cancer, carried out by Russ⁶ and others,⁷ in the cancer research laboratories of the Middlesex Hospital, but this would seem one of the most hopeful lines of research yet opened up. Certain it is that a definite, and perhaps permanent, immunity to grafted cancer has been conferred on a considerable number of rats by inoculation with irradiated tumour tissue.

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A VERY EARLY CASE OF GUMMA OF THE ILEUM.

BY

G. A. UPCOTT-GILL, AND H. B. JONES, M.R.C.S.,
F.R.C.S. EDIN., L.R.C.P. LOND.,
MEDICAL SUPERINTENDENT, RESIDENT SURGICAL OFFICER,
QUEEN'S HOSPITAL, FROGNAL, SIDCUP.

THE case described was considered worthy of being placed on record as an example of very early gumma of the ileum and also a pathological rarity. It will be recalled that in the whole intestinal tract the rectum is the commonest site for specific lesions, and that next in order come the lower part of the jejunum, the colon, the duodenum, and the stomach, in that order.¹

But there are so few records of gumma of the ileum that it is not unreasonable to conjecture that such lesions occur more frequently than is supposed, and may be subjected to surgical interference under a mistaken diagnosis.² The details of the case are as follows:

T. C. C., male, aged 45, married, in 1916, while serving with the Royal Engineers, complained of pain and swelling in the left foot and ankle, and subsequently both wrists and the right ankle, these being treated as rheumatism. Coincidentally with this condi-

tion he first complained of colicky pains in the abdomen associated with vomiting of pale green material streaked with blood, and stated that the vomiting relieved the pain. Later these symptoms increased in severity, with marked distension around the umbilicus and with offensive motions.

First Laparotomy.

On July 10th, 1916, at the 1st General War Hospital, Birmingham, an exploratory laparotomy was carried out. The medical case sheet had the following entry: "Divided adhesions between omentum and gall bladder. The small intestine two feet above the ileo-caecal valve was congested and thickened, and a few mesenteric glands were enlarged. Two feet of small intestine was removed and lateral anastomosis made between the proximal end of the ileum and transverse colon. Appendix was normal."

When discharged from hospital two months later, the patient's condition showed little improvement. In March, 1917, there was a severe attack of haematemesis and rectal haemorrhage of bright red colour. Since that date he stated that he had had attacks of abdominal pain and vomiting which lasted for two months, and from which he was then free for two months, with anorexia between the attacks.

He was admitted to the Queen's Hospital, Sidcup, on May 17th, 1923, complaining of abdominal pain, stabbing in nature, in the umbilical region and radiating through to the back, most marked on rising in the morning (no relation to food, though vomiting relieved the pain); vomiting, night and morning during the attacks—the vomit consists of a yellow material streaked with blood, and contains apparently undigested food; diarrhoea, constant during the attacks; haematemesis, with rectal haemorrhage; and pain in both wrists, hands, calves, and feet, of a stabbing nature.

Condition on Admission.—Pale, thin man; furred tongue; slight pyorrhoea alveolaris; pharynx red and congested. No focus of sepsis found elsewhere in the body. Has lost weight and looks rather cachectic. No evidence of syphilis on the penis or testicle; suspicious old cicatrices on the front of the right tibia. The patient denied having had syphilis or gonorrhoea, but stated that in 1899 he had a bubo in the groin incised and much pus exuded.

Abdominal examination showed a ventral hernia in the old laparotomy scar, through which marked peristalsis, associated with intestinal distension, was seen. Tenderness and rigidity over the epigastric and right hypochondriac regions. No tumour was felt, and no enlargement or displacement of the liver or the kidneys detected. All abdominal reflexes absent. On rectal examination no haemorrhoids, ulceration, enlarged prostate, thickened vesiculae seminales, or any other abnormality could be detected.

A report after a bismuth meal and examination by x rays stated that the stomach appeared normal in size and position. Incisura observed which did not disappear on massage, but no corresponding tender spot.

No parasites or amoebae were found in the faeces after repeated examinations; no visible blood. The benzidine reaction was positive. Examination of the urine showed nothing abnormal.

Central nervous system: Knee-jerks absent; ankle-jerks absent; plantar reflex normal. Eyes react sluggishly to light and accommodation. No areas of hyperaesthesia or anaesthesia noted; no Rombergism. Patient complains of rheumatic pains in the muscles of both calves. No loss of sense of position.

On examination of the blood nothing abnormal was detected except a marked eosinophilia (9 per cent.). The coagulation time was normal. The Wassermann test was positive.

Second Laparotomy.

A second exploratory laparotomy was carried out on July 10th, 1923. On opening the peritoneal cavity much dense fibrous tissue was encountered. No anastomosis of the bowel was discovered, but in the ileum, two feet from its termination, the following condition was found: a clean-cut injected segment of gut, 3 inches long, involving the whole circumference, the centre of which was thickened and boggy, with well defined edges, and apparently enlarged lymphatic glands, and dilated lacteal vessels at its mesenteric attachment. On attempting to invaginate the bowel with the examining finger, it was evident that the lumen was diminished. The mesentery elsewhere showed occasional small white plaques without induration, and the appendices epiploicae were pearly white in appearance. There was no free fluid in the peritoneal cavity. The gastro-intestinal tract elsewhere and the liver, spleen, kidneys, pancreas, and gall bladder all appeared normal.

In view of the condition found it was felt that further surgical interference was not warranted, and the abdomen was therefore closed in the usual way. The matting of the bowel and the omentum precluded a thorough search for further intestinal lesions, and it is possible that others existed, and have given rise to the long-drawn-out symptoms from which this patient has suffered. It may also be noted that usually old gummatous lesions of the gut are associated with hepatic infection and definite ascites, but neither of these conditions was present in this case.³

Resection was not carried out for fear of sloughing at the site of the anastomosis; as it was, the abdominal wound did not heal by first intention, but showed the characteristic non-union seen in specific wounds.

An intensive course of antisyphilitic treatment is now being carried out and the patient's condition is improving markedly; in fact he states that he never felt better in his life.

CONCLUSIONS.

Practically the only other conditions with which this might be confused are dysentery (amoebic or bacillary), tuberculosis, and new growth. The want of any history of dysentery, the repeated negative reports on faecal