level of the eleventh intercostal space. It is in this direction that effusions from ruptured gastric or even duodenal ulcers are directed by the slope of the mesial watershed and the presence of the mesocolic shelf." Hunt² records an abscess confined to the lesser sac of the peritoneum with which a duodenal ulcer communicated directly; such an abscess would extend into the left side of the abdomen.

REFERENCES.

¹ Box, *Lancet*, London, 1910, i, 851. ² E. R. Hunt, *Trans. Med. Soc. Lond.*, 1905, xxviii, 76. ³ Moynihan, *Duodenal Ulcer*, 1910 (W. B. Saunders Company).

ON THE TRANSMISSION OF LEPROSY TO ANIMALS BY DIRECT INOCULATION.

By H. BAYON, M.D.,

BEIT MEMORIAL RESEARCH FELLOW.

(From the Lister Institute of Preventive Medicine.)

APPARENTLY there exists the widespread opinion that leprosy has never been transmitted to animals by means of direct inoculation of nodules from the human being. In fact, Abraham, in his careful and comprehensive chapter on leprosy in Allbutt and Rolleston's *System of Medicine*, after reviewing the various attempts to inoculate animals, comes to the conclusion that

The evidence given above, though to some extent conflicting, may on the whole be regarded as supporting the view expressed by Besnier—that leprosy is strictly a human disease which cannot be transmitted to animals.

I need not refer to the similar views held for many years regarding syphilis, which, being a disease due to a protozoon-like germ, might possibly be specific for the human race, as appears to be the case with malaria in man. And yet, after Bertarelli and Parodi succeeded with their first experiments, no one seems to have found it impossible to transmit syphilis to the rabbit.

Leprosy is a disease due to a definite bacterium, and there appears to be no special reason why the rabbit or any other laboratory animal should not be inoculable with it. The existence of spontaneous rat-lepra affords, in fact, the best ground for postulating the possibility of transmitting lepra to animals.

However, in a matter like this it is useless to quibble with words about possibilities. All arguments can be swept aside by the statement of successful inoculation, supported of course by detailed histological evidence.

I am not taking into consideration the infection of animals with leprosy after cultivation of the germ.

Rost has reported that he has produced the clinical features of leprosy in a monkey by injecting his streptothrix.

Duval, by injecting his strain of *B. leprae* in enormous quantities into a monkey, produced lesions which, he says, could not be distinguished from those in the human being. Kedrowsky has produced in mice and rabbits lesions extremely similar to those of human leprosy by injecting the germs he cultivated from lepers. I have had an opportunity of examining his microscopical slides personally, and admit that they are most convincing.

With a diphtheroid-like germ cultivated from a leper I have produced lesions in a mouse indistinguishable from those occurring in spontaneous rat leprosy.

Now, however, I am concerned with reviewing the work done by grafting lepromata to animals direct from the patient. So far as I can gather from the literature on this subject the positive results which have been recorded are as follows:

1881. Neisser, after twenty-four unsuccessful attempts on rabbits, injected two dogs with leprosy nodules, and concluded from the results that leprosy developed locally at the site of inoculation.

1883. Damsch grafted lepromata in the anterior eye chamber of two rabbits. The animals died after 139 and 219 days. Apparently a slight increase in the quantity of acid-fast germs had taken place. He also inoculated two cats in the abdomen with leprosy nodules. After 120 days numerous bacilli were found in the newly formed tissue round the atrophied nodules.

1888. Vossius carried out experiments in a similar fashion to Damsch on rabbits and had identical results.

He also considered that the acid-fast germs had multiplied.

1885-6. Melcher and Ortmann inoculated four rabbits in the same way. They succeeded in getting, after four to ten months, definite metastases and deposits of acid-fast germs in the spleen, liver, caecum, pleura, and pericardium. They stained these germs with Baumgarten's differential stain and found that they had the staining properties of Hansen's germ.

1887. Wesener injected several rabbits with leprosy nodules, and in two animals out of eight, after periods of four and a half months and eight months respectively, he found lesions apparently identical with those described by Melcher and Ortmann—that is, nodules from the size of a pinhead to that of a pea in the lungs, on the pleura, on the epiploon, in the liver, in the lymphatic glands, spleen, kidneys, caecum, and peritoneal surface. Caseation and giant cells were present. In the eyes of the rabbits he obtained after six and eight months a congregation of round cells choked up with acid-fast germs. He considered that the generalized lesions were due to tuberculosis and that the ocular lesions were caused by dead bacilli, because acid-fast germs can be demonstrated in the eye of the rabbit after inoculation with nodules which have been kept for years in alcohol.

1901. Barannikow confirmed these results on one rabbit.

1893. Wnoukow inoculated twenty rabbits with leprosy nodules in various fashions (intraocularly, subcutaneously, intraperitoneally). In fourteen rabbits he got lesions which he considered to be of tuberculous nature. No confirmatory tests with guinea-pigs appear to have been made.

1893. Tedeschi inoculated a leproma into the dura of a monkey. The animal died after eight days; that is far too brief a period for any conclusions to be drawn.

1902. Ivanow injected several guinea-pigs with leprosy nodules. In one case the animal was killed after eight months and found to have nodules in the epiploon, which Ivanow considered were due to multiplication of the bacilli.

1905. Thiroux inoculated five rabbits with leprosy material. The animals lived thirteen to twenty months and presented various lesions at autopsy, which Thiroux considered to be tuberculous.

1906. Nicolle inoculated monkeys with ground-up nodules and succeeded in getting localized lesions.

1909. Marchoux and Borret inoculated a chimpanzee under the skin of the ear with a freshly-excised leprosy nodule. It apparently increased in size during three months and then began to be resorbed. An examination of the blood showed a few leucocytes with badly-staining bacilli. The animal died ninety-six days after inoculation. The nodule had reached the size of a split pea, and under the microscope was shown to consist of three layers. In the middle were the remains of the original tissue, quite necrosed, with a few loose acid-fast germs. Around this was a considerable number of lymphocytes, enclosing numerous bacilli, and at the periphery organized connective tissue with a few cells filled with bacilli. The authors considered that a proliferation of the original germs had taken place.

1909. Sugai inoculated Japanese dancing mice intra-peritoneally with an emulsion of fresh leprosy nodules and found as a result the development of milary granulomata on the peritoneal lining, especially in the hepatic region and epiploon. Also the bronchial and peritoneal glands showed characteristic leprosy lesions. All contained acid-fast germs. The attempt to transmit the disease from these to other mice failed.

1909. Kitasato appears to have successfully inoculated an orang-outang on the cornea. Only scanty details were, however, given.

1909. Stanziale reports upon some very careful and thorough experiments on rabbits. In one typical case he inoculated into the eye of the animal a fragment of leproma. During the first few days a marked hyperaemia developed round the opening in the cornea. Soon afterwards a constant diminution in the size of the nodule could be made out, accompanied by the formation of an opalescent exudation, which took its departure from the inoculated piece of tissue and spread out as a fan-shaped segment. After twenty days the nodule became stationary

and remained so during fifteen to twenty days without any noticeable change taking place. After forty days the nodule began slowly to increase till it had tripled its original size. In the same time small grey nodules made their appearance and could clearly be distinguished on the surface of the inoculated tissue. These little nodules attained the size of a pin's head. Some appeared to be adherent while others were loose and independent. After the initial hyperaemia due to the operation had disappeared, a new formation of blood vessels took place, which spun a delicate network round the piece of tissue inoculated. After seventy days the rabbit's eye was enucleated, part of the tissue was used for histological observations and the rest was grafted into the cornea of two other rabbits. In one the graft got resorbed without any further results in the course of two months. In the other rabbit the graft began to increase in size after fifty days and produced similar changes to those described in the foregoing animal. The experiments are being continued by the author, but to date the results obtained are: thirty-one rabbits have been inoculated and in eight it was possible to produce leprosy ocular lesions. In some of the positive cases the material was taken eighteen to nineteen hours after excision from the patient. In all cases in which the inoculation succeeded the Wassermann reaction was positive. As a control Stanziale inoculated lepra nodules into the abdomen of another rabbit and found at intervals after a month the reaction constantly negative. The same negative result was achieved after grafting into the cornea of rabbits pieces of human skin or dead leprosy nodules.

These experiments of Stanziale have been most carefully carried out, and full descriptive details are given.

1911. Duval inoculated a series of animals—namely, four rats, four white mice, and four Japanese dancing mice—with grumous material taken from an acute case of human leprosy which had developed numerous soft subcutaneous leprosy masses and had repeated attacks of leprosy fever. A small quantity of material was used in each case—namely, 0.5 c.cm. emulsified in 1 c.cm. of normal saline solution. Some were injected intraperitoneally, others subcutaneously.

The two white mice which received intraperitoneal injections died fourteen days after the inoculation. At the autopsy both showed a general infection of the peritoneum with a pure growth of the *B. leprae*, while the mesentery, omentum, visceral and parietal peritoneum contained numerous minute, firm greyish-white nodules, which on microscopic section proved to be typical leprosy lesions. The most surprising feature was the occurrence of a slightly turbid, semigelatinous exudate, which microscopically consisted almost entirely of large mononucleated cells (macrophages). Great numbers of these cells were filled with acid-fast bacilli, and scarcely any were found that did not contain a few. No remarks are made about the other animals.

1911. Couret fed two goldfish on teased nodules from a leper. No other food was allowed the animals until they had disposed of the leprosy tissue, after which they were cleansed and transferred to a clean aquarium.

The first was examined twenty-four days later; acid-fast organisms had not been found in the faeces for three days before the animal was killed. No evidence of infection was apparent externally or internally. Films made from the omentum and other organs showed a few scattered acid-fast bacilli. The average number of bacilli to the slide was about four, and no change in morphology was seen. The second fish was examined after thirty-seven days. The findings were similar to those in the first one. With reference to these experiments it should not be forgotten that tap water appears to harbour acid-fast germs frequently, as shown by Brehm, Beitzke, Schern und Dold. The tap water at the Lister Institute also contains acid-fast germs.

My own experiments on this question are as follows:

I injected four rats on two occasions in the testes with ground up nodules from a case of leprosy from Mauritius. Two rats did not show any macroscopic lesions, even after four months. One rat, however, developed, four weeks afterwards, a nodule at the site of inoculation, which grew to the size of a small pea. On puncture it showed acid-fast germs and necrosed tissue, some of which I do not doubt represented the original cells injected. After five

weeks the rat died,* and I injected the whole of the nodule subcutaneously into two other young rats. Quite lately, that is, three months after inoculation, one of the rats is losing fur on the surface of its abdomen, without there being any signs of the usual rat scabies about the ears or tail. Small shotty nodules are felt under the skin.

Another rat developed now, three months after the second injection, a nodule in the left testis. This broke down, and was found to contain acid-fast rods in great quantity. I cannot decide so far if a multiplication of the lepra germs has taken place. I do not intend admitting a multiplication till definite metastasis can be found in other organs, and not only germs at the site of injection.

However, taking into careful consideration the literature I have quoted, I come to the conclusion that leprosy is directly transmissible to rats and rabbits from the human being; that, however, a very long time of incubation must be allowed for, and very many unsuccessful attempts and partial results are to be expected, as has been the case in my experiments.

I consider the results of Melcher and Ortmann, Wesener, Wnaukow, Stanziale to have been successful. Spontaneous tuberculosis in laboratory animals is extremely rare. During ten years I have not seen a single case, and the experience of other workers I have asked is similar to mine.

It is quite true that lepra "bacilli" are so quiescent, and cause such minimal reactions in the tissues they invade, that it is not possible to distinguish whether they are dead or alive, the word "alive" being taken in the sense of "capable of multiplying." We have no other method of deciding whether an acid-fast germ is living or killed but that of testing its capacity for multiplication on a laboratory culture medium. And this has been for many years a controversial point with leprosy, because no culture so far has succeeded in reproducing anything like leprosy lesions in the animals experimented upon. Lately, however, Kedrowsky has published drawings and photographs of microscopical sections which leave little doubt that he has succeeded in producing in rabbits and mice lesions indistinguishable from those occurring in leprosy of the human being. I have now been working with this germ for over a year and have not been able to find any evidence that did not speak in favour of its being leprosy.† This germ produces in the liver of rabbits and in guinea-pigs lesions which, taken singly and separately from the others, might be mistaken with the chronic type of tuberculosis which occurs in rabbits and very exceptionally in guinea-pigs, and which can easily be imitated by the intravenous injection of an avian strain into rabbits. This appears to me to also be circumstantial evidence in favour of leprosy having been inoculated on several occasions to rabbits. The lesions were wrongly taken to be tuberculosis.

With regard to Campana's and Wesener's experiments, we must bear in mind that in the analogous disease in rats, genuine or spontaneous rat leprosy, we also find the incubation extremely long, up to seven months, and one is often in doubt whether the bacteria found in the lesions have multiplied or are the original ones injected. And yet there is not much doubt possible that in many cases we succeed in transmitting the disease by inoculation through several generations. My conclusions, therefore, are that:

1. Leprosy can under certain circumstances be transmitted to animals, the main difficulties being the high percentage of unsuccesses and the long incubation.
2. The most suitable animals appear to be the rabbit, rat, or mouse. In the rabbit the intraocular method is preferable. The resulting lesions are often not visible to the naked eye, and are similar to those caused by certain strains of human tubercle.
3. In the rat the incubation is also very long, the resulting lesions comparable to those occurring in spontaneous leprosy of the rat.
4. Not all leprosy patients' nodules are equally "infective" for animals. In some cases the lepra

* I can add that no acid-fast germs were found in the organs of this rat. Microscopical sections were made of liver, spleen, and testes. The disease, if transmitted, was localized.

† I cannot in this paper describe the serological and experimental tests I have carried out with Kedrowsky's germ. It is an actinomycete-like bacterium, and in its acid-fast stage morphologically identical with the "bacilli" found in the serum and pus of lepers.

"bacilli" appear to be absolutely incapable of multiplication, for reasons we do not at present know.

5. According to Stanziale's experiments, the "Wassermann reaction" is positive in rabbits which have successfully been inoculated.

Memoranda :

MEDICAL, SURGICAL, OBSTETRICAL.

INTESTINAL OBSTRUCTION FROM AN UNUSUAL CAUSE.

ON a Saturday a few months ago I was called to see a girl about 18 years of age. She had been in good health until the previous Sunday, when, just before dinner, she ate an orange, skin and all. Shortly afterwards, she was taken with severe pain, followed by vomiting and diarrhoea, which lasted until the following Thursday, her mother informing me that an orange always upset her in this way. On the Friday the pain was more severe and the vomiting persistent.

When I saw her she complained of great abdominal pain, and said she could retain nothing. The bowels had moved the previous day, and she had been passing flatus since.

Photograph (exact size) of foreign body made up of bits of gutta-percha, matted together and blocking top ileum, causing intestinal obstruction.

There was considerable abdominal tenderness, more particularly on the right side. This condition continued until on the Monday there was distinct faecal vomiting. An operation, however, was refused. On the following day the patient's condition was much worse—constant vomiting with abdominal pain—no movement of the bowels in spite of repeated enemata, but passage of flatus. The patient was removed to the hospital. I opened the abdomen the same evening, and on introducing my hand into the abdominal cavity I felt a hard mass like a stone in the pelvis. This mass was found to be blocking the ileum, about six inches from the ileo-caecal junction. I removed the lump through a longitudinal incision in the ileum, and on examination found it to consist of small bits of gutta-percha matted together.

The girl works in a safety-fuse factory, and her duty is to supervise the coating of the fuse with melted gutta-percha. This is contained in little cups through which the fuse passes, and the girl's duty is to keep these cups filled with gutta-percha from a container; this is done by means of a large spatula. Some of the gutta-percha naturally adheres to the spatula, and the girl had been in the habit of cleaning the spatula with her fingers, and then removing the gutta-percha adhering to her fingers with the teeth, and chewing and swallowing it.

The photograph is the exact size of the lump removed, and the different colours are explained by the fact that some of the gutta-percha is mixed with bitumen, giving it a black colour, and some is not.

The patient made an uninterrupted recovery, and is now at work again.

Camborne.

J. TELFER THOMAS,
L.R.C.P.Lond., M.R.C.S.Eng.

THE Royal Society will celebrate its 250th anniversary this year on July 16th.

SURGEON-GENERAL W. J. FAWCETT, C.B., A.M.S., retired pay, has been appointed a Deputy Lieutenant for the County of Leitrim, and a Justice of the Peace for the same county.

THE President of the United States has sent to the Senate the nomination of Dr. Rupert Blue, of South Carolina, as Surgeon-General of the Public Health and Marine Hospital Service, in succession to the late Dr. Walter Wyman.

Reports

ON

MEDICAL AND SURGICAL PRACTICE IN THE HOSPITALS AND ASYLUMS OF THE BRITISH EMPIRE.

UNIVERSITY COLLEGE HOSPITAL.

A CASE OF CRANIO-SPINAL MENINGITIS, WITH RIGHT-SIDED
HYDROCEPHALUS SIMULATING INTRACRANIAL TUMOUR.

(Under the care of Dr. BATTY SHAW.)

[Reported by TREVOR BERWYN DAVIES, B.Sc.Wales,
M.D., B.S.Lond., late House-Physician.]

FLORENCE J., aged 4½ years, was admitted into University College Hospital on February 14th, 1910; the following history was obtained from the mother:

HISTORY.

The illness began eight weeks before admission with irritability and frontal headache; the patient cried out at times with the pain in her head, while in the intervals between the crying she was rather drowsy and resented interference. The appetite, which had been good, now became very poor, and the patient began to vomit; this was unrelated to food and came on at intervals of two to three days, the vomited matter consisting of clear non-blood-stained fluid, about one teacupful in quantity being forcibly shot up on each occasion. The bowels were fairly regular up to nine days before admission, but had since been obstinately confined. During the week before admission the mother noticed that the child had a squint. The patient had been gradually getting thinner and weaker. She had had bronchitis and measles when 2 years of age, and whooping-cough when 3 years old. She had been breast-fed and was always a bright child, although her mother says she had noticed twitchings and convulsive movements at times ever since birth. The patient had begun to go to school in October, 1909.

There was a history of three miscarriages in the mother, and of two other children dying a few hours after birth, while another child died of diarrhoea and vomiting when 15 months old. The patient had one brother alive and well.

STATE ON ADMISSION.

The patient is a thin, poorly-nourished child, lying on her right side, with the legs drawn up. She is irritable and cries when touched, and yawns frequently. The temperature is 99.4° F., pulse 136, and respirations 28 per minute. The heart and lungs are normal. Faecal masses can be felt in the abdomen.

Central Nervous System.

The pupils are equal, reacting well both to light and accommodation. There is double optic neuritis, that on the right side being the more marked. Both external recti are paralysed, and there is also coarse nystagmus present. The remaining cranial nerves are normal.

Limbs.—There is no rigidity, paralysis, or tremor. Kernig's sign is absent, and there is no *tache cérébrale*. The reflexes are normal in the upper limb, but in the lower limbs the knee-jerks are both absent, and there is well-marked extensor response on both sides. There is no ankle clonus. The sphincters and sensation are normal. The gait could not be observed.

FURTHER HISTORY OF THE CASE.

Lumbar puncture was done on February 15th and revealed 4,900 white cells per cubic centimetre, 71 per cent. of which were small lymphocytes. Extracellular Gram-negative diplococci were found. No tubercle bacilli were found, and von Pirquet's reaction was negative.

The bowels were opened daily with enemata, and the patient began to improve a little, both in intelligence and spirits. By the end of a week (February 21st) she was able to walk. The gait was somewhat reeling, with a tendency to fall to the right side; she walked with a wide base. Rombergism was well marked. The physical signs were much as before, except that the right knee-jerk could