

A note on an experimental investigation into the pathology of cancer / by Charles A. Ballance and Samuel G. Shattock ; communicated by Sir James Paget.

Contributors

Ballance, Charles Alfred, Sir, 1856-1936.
Shattock, Samuel George.
Royal College of Surgeons of England

Publication/Creation

[London] : [Royal Society of London], [1890]

Persistent URL

<https://wellcomecollection.org/works/xnjnqnhv>

Provider

Royal College of Surgeons

License and attribution

This material has been provided by This material has been provided by The Royal College of Surgeons of England. The original may be consulted at The Royal College of Surgeons of England. where the originals may be consulted. This work has been identified as being free of known restrictions under copyright law, including all related and neighbouring rights and is being made available under the Creative Commons, Public Domain Mark.

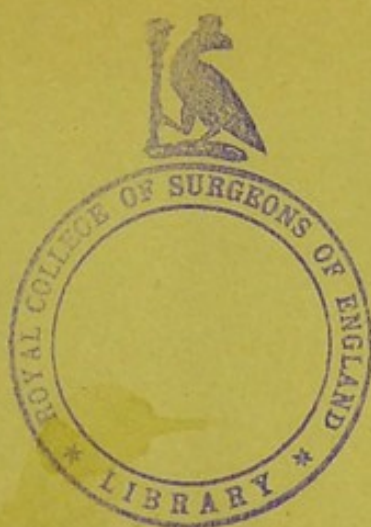
You can copy, modify, distribute and perform the work, even for commercial purposes, without asking permission.



Wellcome Collection
183 Euston Road
London NW1 2BE UK
T +44 (0)20 7611 8722
[E library@wellcomecollection.org](mailto:Elibrary@wellcomecollection.org)
<https://wellcomecollection.org>







8

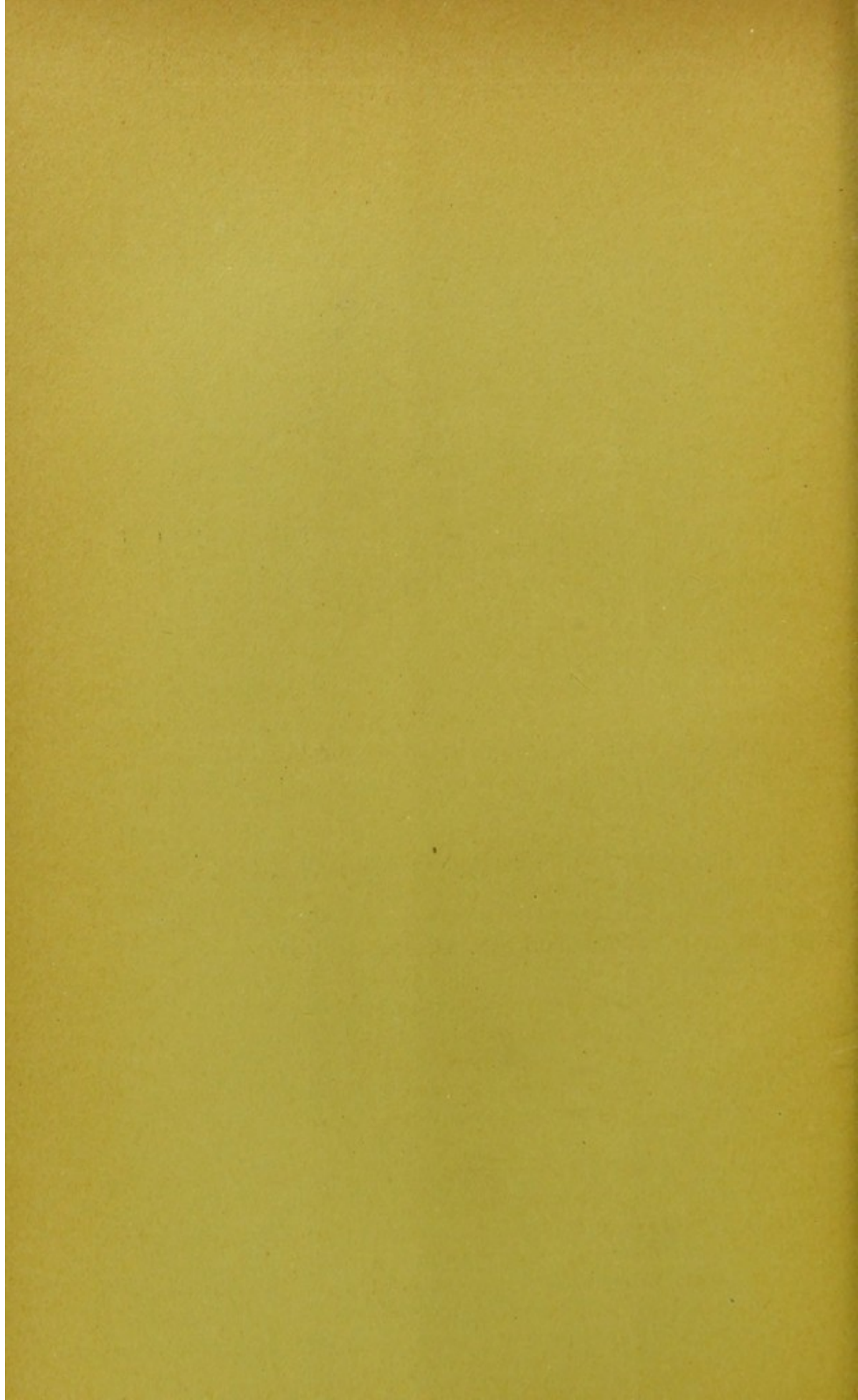
A NOTE ON AN EXPERIMENTAL INVESTIGATION
INTO THE PATHOLOGY OF CANCER.

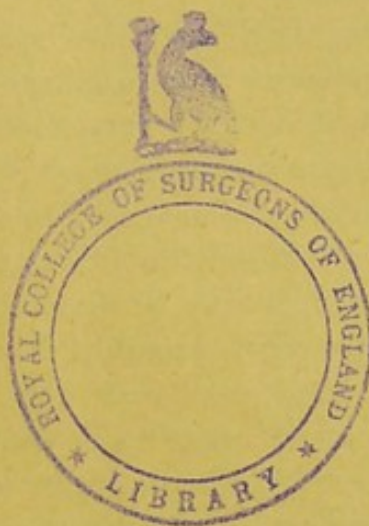
BY

CHARLES A. BALLANCE

AND

SAMUEL G. SHATTOCK.





“A Note on an Experimental Investigation into the Pathology of Cancer.” By CHARLES A. BALLANCE and SAMUEL G. SHATTOCK. Communicated by Sir JAMES PAGET, Bart., F.R.S. Received April 15—Read May 1, 1890. Revised June 10, 1890.

Our first method of conducting the enquiry was by seeing if any special micro-organism could be artificially cultivated from malignant tumours, such as can be done from tubercle, and the pathological formations of certain other infective diseases.

These experiments were made in most instances with carcinomata of the breast, and in a manner fully detailed in the ‘Pathol. Soc. Trans.’ vol. 38. We thus experimented with three lipomata, one myxoma, three sarcomata, and about thirty carcinomata.

The results yielded by this particular method, and the particular cultivating media mentioned, may be described in a single word as negative.

We have been able to keep portions of many carcinomata sterile for an indefinite time after various periods of incubation up to thirty-three days; and in one case, in which fluid human serum was employed, the incubation was continued for 134 days.

The pieces transferred to solid media which remain sterile undergo no change perceptible to the naked eye. We have at the present time (February 20th, 1890), amongst others, a piece of a

carcinoma of the mamma 1 inch in length, which was placed on agar immediately after the excision of the tumour on May 12th, 1887. It was incubated at 100° F. for some days and has since been kept in a warm cupboard. It does not even now show any naked-eye change and looks as though it had just been removed.

By the same method we showed the absence of micro-organisms in healthy living tissues.

Notwithstanding such negative results, we do not by any means think that the evidence from analogy that cancer is probably micro-parasitic in origin is hereby overthrown. For of the micro-organisms already known, some are very selective in regard to artificial culture media, others whose existence admits of easy microscopic demonstration have as yet withstood the efforts made to cultivate them without the body. Moreover, it may be allowable with respect to the parasite itself to conjecture that possibly it does not belong to the Protophyta, but to the Protozoa; in which case the difficulty of artificial culture would be easily explained; and the enormous rapidity of cell growth in cancer might be thought of as being induced by a cancerous rejuvenescence setting in in consequence of the conjugation of the "parasite" with the cells of the normal tissues.

And so the culture medium in the case of cancer, it may be, has yet to be found.

Human blood serum apparently offers the most likely chance of success, and with it we have made some experiments. We have obtained human blood serum from fresh placenta by the method of expression, and have employed it, both liquid and inspissated, at blood heat. After some experience we found it best to have the blood collected in sterile bottles directly from the divided cord whilst the placenta was as yet unexpelled. However, no growth has occurred under sterile conditions either when the serum has been simply inoculated or when a piece of living cancer has been placed in or upon it. The tubes were kept in the incubator for some weeks. The same result has also attended the use as a nutrient soil of fluid or inspissated human hydrocele fluid; *e.g.*, a piece of scirrhus was incubated for eight days on inspissated hydrocele fluid, after which it was kept at the temperature of an ordinary living-room. It has remained sterile and without appreciable change to the present date, twenty months since the experiment was performed.

Abstract of Three of the Experiments with Human Placental Serum.

Experiment 1. Scirrhus of the Breast.—Pieces of the tumour were cut with knives which had been wrapped in cotton wool and heated on a previous day in the "iron box" for an hour in the hot-air steriliser at 150° C. The pieces thus cut were put into two tubes of

human placental blood serum discontinuously sterilised and inspissated.

The blood collected, as previously stated, was poured into long sterilised test-tubes, which were allowed to stand in cold water and plugged with sterilised wool. The following day the serum was drawn off with a pipette and transferred to other sterilised tubes plugged with wool. These were then placed on six successive days in a serum steriliser, and some of them afterwards were solidified. The blood furnished from a single placenta was not more than sufficient to charge two or three tubes. Into two tubes, as above stated, of solidified serum thus prepared were placed pieces of the above tumour. One of these showed a white coccus growth on the seventh day; the other remained sterile, and was incubated at blood heat for three months. It was then prepared for the microscope. The microscopic sections show distinct "budding" of both epithelial and connective-tissue cells.

Experiment 2. Large Recurrent Carcinoma of Breast. Woman, æt. 30.—Into three tubes of fluid human placental serum were placed pieces of the growth about half an inch in longest measurement. Into three other tubes of solidified human placental serum were placed three other pieces of the growth after the fluid (expressed at the time of solidification) had been poured off. These last three tubes were then partly filled with fluid human placental serum, previously warmed, and prepared as described under Experiment 1. All these tubes were incubated at 100° F. Three weeks later, cover-glass preparations from the tubes showed in all a variable degree of coccus growth. The vitality of the organisms was tested by inoculating tubes of nutrient jelly. In all cases an iridescent growth occurred which when examined proved to be of coccus form. We were surprised at all the tubes showing a growth, and intend to make some further observations on the micro-organism.

Experiment 3. Small Carcinoma of Mamma.—Woman advanced in age. Into three tubes one of fluid human placental serum and two of nutrient agar with 6 per cent. glycerine were placed pieces of the growth. Incubation at 100° F. On the eighth day one of the agar tubes showed a "white growth" which was found to be a staphylo-coccus. From each of the other tubes a tube of nutrient jelly was inoculated. A fortnight afterwards neither of these jelly tubes showed any growth. On the eighth day the sterile piece of cancer on agar was transferred to Müller's fluid; on microscopical examination it showed typical capitate processes projecting from the nuclei of many of the epithelial cells, as also free granules in the alveoli; some also of the connective-tissue cells show typical budding. These appearances are not visible in sections of a portion of the same tumour which was hardened in a like manner but not incubated.

The piece of tumour submerged in fluid human placental serum was incubated at 100° F. for 134 days. It is wedge-shaped, about half an inch in longest measurement, and appears now at the end of 134 days quite unchanged; the serum, moreover, is clear and unaltered.

Certain appearances presented on microscopic examination by the portions of the tumours which had remained sterile after various periods of incubation at 100° F. are recorded and figured in the 'Pathol. Soc. Trans.,' vol. 39. These consisted in the extrusion of the chromatin from the nuclei in the form of bud-like processes which ultimately appeared to become free of the cells. Similar appearances were observed in sections of cancerous tumours which had not been incubated, but we failed to observe them in normal tissues which had remained sterile on nutrient media, whether incubated at 100° F. or not.

Transplantation Experiments.—Having carried out a large number of bacteriological experiments from the point of view of the possible infectious nature of cancer, it was necessary to proceed with the inquiry in the direction of inoculation or transplantation experiments on brutes with living cancerous tissues. Wild animals are exempt apparently from the ravages of this disease; but those domesticated not rarely fall victims to it.

Plan of Experiments.—The tumour, immediately after its severance from the body of the patient, was placed in a small incubator at 100° F., and conveyed in a cab to the Brown Institution. There it was allowed to stand in a large incubator, while the animal in whose body it was to be grafted was etherised.

The operation was conducted with strict antiseptic precautions. When the peritoneum had been opened, one of us (S.) took the tumour from the incubator and with a sterilised knife or scissors carefully removed all superfluous tissue (*e.g.*, breast tissue and fat). The whole tumour was then transferred to the abdominal cavity, or several portions were cut from it and pushed in different directions with the finger within the peritoneum. In some instances a piece was fixed by fine catgut in the centre of a muscle (*e.g.*, the biceps), the muscular tissue being brought together with catgut over it, and in a third series of experiments portions of tumour with more or less of the surrounding tissues were placed in the subcutaneous tissue or in the subperitoneal tissue.

We avoided the use of tumours that were ulcerated, for we discovered that, even with very slight surface ulceration, the deeper parts of the tumour (even at 1½ or 2 inches distance) gave an abundant growth in a gelatine tube. As a rule, the operation wounds ran an aseptic course, and the animals were not inconvenienced at all. In a few cases in which the tumours were discovered afterwards to be on the verge of breaking down, septicæmia set in, and the brutes were killed with chloroform.

The tumour tissue was transferred to the body of the animal in from a half to one and a half hour after removal. In the interval it was kept at 100° F., so that its component elements probably maintained their vitality practically unimpaired.

In all cases a small piece of the tumour was placed immediately after the transplantation in Müller's fluid, and subsequently prepared for microscopical examination. In some of the experiments the tumour was large enough to allow also of a small piece or pieces being incubated on blood serum. These were afterwards examined with high powers of the microscope if they remained sterile.

The discovery of the nuclear particles to which we have ventured to give provisionally the name of cancer sperm or carciñoza, made us anxious to "graft" with pieces of cancer in which this peculiar nuclear state had been induced. This was done without allowing the selected pieces of cancer to cool below blood heat from the time of their removal from the patient to their lodgment in the body of an animal.

So far all the experiments have yielded negative results; but the life history of cancer is so long, that we think, until the animals have survived for at least two years subsequent to the transplantation, it is impossible to know whether they have been infected or not. That this view is tenable and not improbable, is supported by the instances of those diseases, such as actino-mycosis, in which there is no sign of infection at the inoculated spot until very many months have elapsed. In making this statement, we are cognisant of the experiments in which carcinoma is said to have been transferred from one animal to another of the same species; *e.g.*, Hanau, of Zurich,* transferred squamous carcinoma from one rat to another, the inoculated animal dying within three months of the disease.

All our results up to the present time, with human cancer as far as infection is concerned, have been negative. In those animals that have died, the lump of tumour, if small, has been nearly or quite absorbed, or, if large, an ordinary inflammatory capsule has been found surrounding it, and the tumour tissue itself apparently in a state similar to that known as anæmic necrosis.

We preferred the experiments to be of the character of transplantations rather than of inoculations. It appeared that by the method adopted there could be no doubt that living cancerous cells in large numbers were grafted into the animal experimented upon. We have avoided injections into veins, and other doubtful methods, as likely to lead to erroneous conclusions.

* 'Centralblatt für Chirurgie,' No. 42. Dr. Hanau, being in London at the end of March (1890), was kind enough to show us the photographs and microscopical preparations from the rat he had infected, together with sections of the original tumour.

We are much indebted to Mr. Horsley, Professor Superintendent of the Brown Institution, for his kindness in allowing us every facility at the Brown Institution for carrying on our work, and for his ever ready help in many ways and on many occasions.

Short Abstract of the most important of our Transplantation Experiments.

In all the experiments recorded the tumours were removed from the human subject, except in the case of two of the experiments on dogs.

Monkey (1).—Into the abdominal cavity were placed three small pieces of scirrhus carcinoma of breast that had been previously incubated for seven days at 37° C.

Lived 37 days—death from diarrhoea.

After death, the shrunken remains of the grafts were found adherent to the peritoneum.

Monkey (2).—A piece of a scirrhus carcinoma of breast placed in the abdominal cavity; another stitched with catgut into the biceps.

Lived 115 days. Was killed on account of the appearance of a large, lobulated, pinkish swelling at the site of the abdominal wound.

After death, this mass was found by microscopic examination to be a granuloma, in the base of which was a small piece of prolapsed omentum.

No trace of tumour grafts within the abdomen or in the biceps.

Monkey (3).—Transplantation into both biceps muscles and into muscles of outer part of right thigh.

Death from septicæmia on the 6th day.

The tumour was slightly ulcerated. The gelatine tubes showed a rapid and abundant growth.

Monkey (4).—Into the left biceps was stitched a piece of scirrhus carcinoma of the mamma, and another piece into the right thigh. Lived 66 days. Wounds not quite healed. No remains of grafts found. Death from cold.

Monkey (5).—A piece of scirrhus carcinoma stitched into left biceps, and a second placed beneath the skin of the back.

Lived 15 days. Death from cold. Wounds healed.

Grafts encapsuled by connective-tissue, lemon-yellow in colour.

Microscopic sections of the tumour in both situations show it to be the seat of coagulation necrosis. Around the portion in the biceps is a zone of granulation tissue, which is invading the substance of the tumour, the two being intimately mingled at the periphery of the latter. There are no leucocytes or other living cells in the central portion of the graft. Similar appearances obtain in the microscopic sections of the piece of tumour embedded in the subcutaneous tissue of the back.

Monkey (6).—Into the left biceps and beneath the skin of the right side of the chest were placed pieces of a scirrhus of the breast.

Lived 15 days. Death from cold. Superficial suppuration at seat of wounds.

Monkey (7).—Into the abdominal cavity was placed a thick disc of scirrhus about $1\frac{1}{2}$ inch in diameter.

Lived 3 days. Death from intestinal obstruction.

Post Mortem.—No adhesions. Tumour unaltered in appearance.

Monkey (8).—Into the abdominal cavity was placed a whole scirrhus of the breast.

Lived 49 days. Death from diarrhœa. Wound healed. Graft was contained in a circumscribed abscess.

Cat (1).—Into the abdominal cavity was placed an entire scirrhus of the breast, the fat having been clipped off with scissors; the tumour was dipped in carbolic lotion (1 in 100) before insertion. The operation was done within three-quarters of an hour after removal from the patient.

Wound healed by first intention. Animal died 320 days after the experiment. *Post mortem.*—Adherent to the under surface of the liver were the remains of the tumour. This was of a pale yellow colour, and diminished from its original size, very firm in section, fibrous, and presenting islets of softish yellow semi-fluid substance. All the other organs were healthy, except the kidneys, which were granular.

Rabbit (1).—Into the outer muscles of the right thigh was placed a piece of scirrhus of the breast, $\frac{3}{4} \times \frac{1}{4} \times \frac{1}{4}$ inch.

Animal died 541 days later. *Post mortem.*—In the muscle was found a sharply-defined mass, of flattened oval form, 4 mm. in the shorter diameter; this consists of a distinct capsule of fibrous tissue, enclosing particles of hard earthy substance. It would appear, therefore, that the necrosed piece of tumour had undergone calcification. Viscera all healthy; brain not examined.

Rabbit (2).—Into the outer muscles of the right thigh were placed two pieces of a scirrhus of the breast. Lived 6 days. Negative result.

Rabbit (3).—Into the outer side of the right thigh were placed two pieces of scirrhus.

Lived 36 days. *Post mortem.*—The two pieces of scirrhus were lemon-yellow in colour, fairly firm, and in section presented softish yellow areas.

Dog (1).—Into the abdominal cavity was inserted a whole scirrhus of the breast, $1\frac{1}{2} \times \frac{3}{4}$ inch. Superficial part of wound healed by granulation.

Animal quite well 700 days after the experiment. On this day it

was killed. *Post mortem*.—No peritoneal adhesions. No sign of the graft. All the viscera healthy.

Dog (2).—Abdominal section and insertion of a piece of scirrhus $1\frac{1}{4}$ inch in diameter, and $\frac{1}{3}$ inch in thickness. Nine days later the animal was killed with chloroform. *Post mortem*.—Circumscribed abscess around the shreddy remains of the graft adherent to liver and stomach. No peritonitis.

Dog (3).—*1st Experiment*.—Into the abdominal cavity was placed a scirrhus of the breast, $1\frac{3}{4}$ inch in diameter and discoidal.

2nd Experiment.—390 days after the 1st experiment, a whole scirrhus of the breast with some of the surrounding fat was placed in the subperitoneal tissue.

3rd Experiment.—170 days after the 2nd experiment, into the peritoneal cavity was placed a slice of a subperitoneal round-celled chondrifying sarcoma of humerus, $1 \times 1\frac{1}{2} \times \frac{1}{3}$ inch in volume. This was pushed to the right of the middle line, a similar slice being pushed to the left. The slices were cut in the spray, all surfaces previously exposed being rejected. One of the slices included the growing margin of the growth. Is still alive and well, 650 days after the 1st experiment.*

Dog (4).—*1st Experiment*.—Beneath the skin of the right side of the thorax, by means of a valvular incision, was placed a small scirrhus of the breast, about as large as a horse bean, most of the fat having been previously cut away in the spray. Primary union of wound.

2nd Experiment.—240 days after 1st experiment, into the abdominal cavity was placed the greater part of a breast with two scirrhus masses in it. Death six days later from hæmorrhage into the abdominal cavity. *Post mortem*.—No trace of the first graft beneath the skin of the thorax. No tumours in internal organs.

Dog (5).—*1st Experiment*.—Beneath the skin of the back was placed, an hour after its removal from the patient, a square slice ($\frac{1}{2}$ inch along its sides) of a spindle-celled sarcoma taken from amongst the muscles of the thigh.

Wound healed by first intention.

2nd Experiment.—Beneath the skin of the back, 400 days after the 1st experiment, was placed a wedge-shaped piece, about three-quarters of an inch in depth, of sarcoma, including the periphery. This was removed from a tumour filling the zygomatic fossa of another dog, which was kept under ether while the graft was taken, the animal being subsequently killed. Warm saline solution was poured over the piece before its insertion beneath the skin. The

* July 8th.—Animal killed 760 days after 1st experiment. *Post mortem*.—No sign of the grafts. Viscera healthy.

post-mortem on the dog from which the graft was taken showed no growths in any of the internal organs.

The wound healed by first intention and 50 days later no trace of the tumour could be felt. The tumour on microscopical examination was seen to be a small round-celled sarcoma containing many giant cells and undergoing calcification in places.*

Dog (6).—1st Experiment.—Beneath the skin of the side of the chest was placed a piece of scirrhus of the breast 1 inch in diameter and $\frac{1}{4}$ inch in thickness. The tumour was discharged by suppuration and the wound healed.

2nd Experiment.—112 days after the 1st experiment, an entire scirrhus of the breast was placed in the abdominal cavity, the tumour being sliced into three pieces, which were forced into different situations.

320 days after the 2nd experiment the animal was in good health. On this day it was killed. *Post mortem.*—Omentum adherent to linear cicatrix in abdominal wall. No sign of the graft discernible. No disease of any of the viscera.

Dog (7). Into the abdominal cavity was placed a square slice $\frac{1}{2}$ inch along its sides, and $\frac{1}{4}$ inch thick, cut from a tumour which had been a very short while previously excised from the ischiorectal fossa of another dog. A second piece of the same tumour was placed beneath the skin on the right side of the front of the thorax.

Wounds healed by first intention. Animal in good health 270 days afterwards. The tumour on microscopical examination proved to be a squamous-celled carcinoma with cysts.†

Sheep (1).—Beneath the skin of the back under strict anti-septic precautions was placed a square slice from a subperiosteal round-celled sarcoma of the humerus, 2 inches square, and $\frac{1}{3}$ inch in thickness; this was pushed for some inches into the subcutaneous tissue beyond the incision. The piece included at one of its borders the growing margin with the healthy tissues immediately connected with it. Three weeks after the operation there was a fluctuating swelling at the site of the graft, and six weeks after the operation the graft was discharged in the state of necrosis. On the 108th day the animal, apparently in good health, was killed.

Post mortem.—Sheep healthy in every respect.

Sheep (2).—Beneath the skin of the back was placed a slice of scirrhus of the breast with a rim of the surrounding fat, the whole being $1\frac{3}{4}$ inch in diameter and about $\frac{1}{3}$ inch in thickness.

* July 8th.—Animal killed 590 days after the 1st experiment. *Post mortem.*—No trace of the grafts. No sign of cancerous infection.

† July 8th.—Animal killed 400 days after the experiment. *Post mortem.*—No sign of graft. Viscera healthy.

Death occurred about 36 hours after the experiment of ether—collapse of the lungs.

Sheep (3).—Beneath the subcutaneous fat of the back were placed two grafts of a rapidly growing round-celled sarcoma removed from the pectoral region for the third time. The grafts were cut in the spray and then washed in warm sterile salt solution. The larger graft was a thick slice about $1\frac{1}{4}$ inch in diameter, and the smaller was a cubical piece taken from the other half of the tumour. The wound healed by first intention. On the 30th day the animal was quite well, and on palpation no evidence of the grafts could be discovered.*

Besides the above transplantation experiments, we fed two white rats, male and female, with portions of fourteen fresh scirrhus tumours of the breast. In many instances the animals were fed on two successive days with portions of the same scirrhus tumour. These feeding experiments have extended over a period of seven months, and the rats are now alive and well, 250 days from the date of the first experiment. During this time several litters of young rats have been born. These feeding experiments we propose to continue on the same animals. They were undertaken with the view of seeing if infection of the stomach or intestine could be induced in a way similar to that which is set up in some instances by the injection of tuberculous material.

In regard to the literature of the question, Scheuerlen, in the autumn of 1887, read a paper before the Medical Society of Berlin, claiming to have discovered a bacillus in cancer by means of artificial cultures. Francke corroborated this. But subsequent observers, amongst whom is Baumgarten ('Centralblatt f. Bakteriologie u. Parasitenkunde,' vol. 3, No. 13), have shown that these observations were fallacious and due to contamination. Moreover, Rosenbach and Fränkel (at Koch's request) kindly wrote and told us that the swellings induced by Scheuerlen's operations were from their own observations not cancerous.†

Many experimenters have recorded observations with respect to transplantation or grafting of cancer. Here again the results are at

* July 8th.—Animal killed 165 days after the experiment. *Post mortem*.—No sign of local or visceral infection.

In the same way, between three and four months ago, we transplanted living portions of scirrhus tumours into three white rats. At present they show no signs of infection. It may be said, then, that at present there is no evidence that human cancer can be transferred to brutes.—July, 1890.

† Professor Platon I. Kubasoff, of Moscow ('Proceedings of the third General Meeting of Medical Men at St. Petersburg,' 1889, No. 2, p. 41) has asserted that a bacillus can be cultivated on coagulated blood serum which will produce tumours in rabbits and cats after inoculation. It will appear from what is stated in the text that this requires confirmation.

variance. Senger* and Senn† have never observed tumour formation to ensue after grafting. This accords with the results of earlier observers in this field, Sir William Savory and Sir John Simon. In none of these experiments were the animals suffered to live any considerable time, and it is in this that they are not satisfactory. Of carcinoma it is especially true that it is a disease of advancing years.

In experiments made from animal to animal Dautrelepoint obtained only negative results, as also did Senn.

We have already noticed Hanau's successful inoculations of squamous-celled carcinoma of a rat into the abdominal cavities of two other rats; and it remains to mention the transplantation experiments of Dr. Wehr,‡ who successfully transferred a vaginal carcinoma of a dog into the subcutaneous tissue of the belly of another female dog. Valvular apertures in the skin were made in four places and a piece of tumour was pushed into each with antiseptic precautions. The experiment was performed in December, 1887. The nodules increased in size and the animal died in June, 1888 much emaciated. At the autopsy the retroperitoneal glands and the spleen were occupied by secondary growths.

By injecting cancer juice triturated and mixed with distilled water into the jugular vein of dogs, certain results have followed in the hands of Langenbeck, Follin, and Lebert. Nodules have been found in some of the internal organs, but the results are of no value owing to the lack of sufficient histological investigation as to their nature. For it is well-known that inert solid particles if lodging in internal organs excite a local inflammation and production of fibroid tissue, which may attain some size; this is a well-known occurrence in the lung in masons, for instance.

Hahn ('Berlin Klin. Woch.,' 1888) has shown that in the human subject it is possible to transplant a cancerous nodule from one spot to another in the *same* person, with the result of the graft increasing in size and invading the surrounding tissues.

In the 'Progrès Médical,' No. 16 (1889), Darier reports that he has found coccidia in the epithelium in "Paget's Disease of the Nipple." He concludes that not only this disease, but the carcinoma that often follows it, are caused by the parasite; and at a meeting of the Pathological Society (March, 1890), J. Hutchinson, junr., showed specimens which he believed were confirmatory of Darier's observation.§

* "Studien zur Aetiologie des Carcinoms" ('Berlin Klin. Wochenschrift,' 1888).

† "Surgical Relations of Micro-organisms" ('Transactions of the American Surgical Association,' vol. 6, 1888).

‡ 'Transactions of the eighteenth Congress of German Surgeons,' Berlin, 1889, "Weitere Mittheilungen über die positiven Ergebnisse der Carcinomüberimpfungen von Hund auf Hund."

§ Neisser, in the 'Viertelj. f. Derm. u. Syphilis,' 1888, expresses his belief that

Whether the carcinoma which follows in certain cases of Paget's disease is caused by these organisms, which presumably produce the cutaneous lesion, remains open for future investigation, as does also the question whether there are in cancerous tumours generally parasites of the same, or of an allied, nature, but which from their similarity to the cells of the infected tissues have hitherto escaped notice.

molluscum contagiosum is a disease due to the presence of Psorozoa; and both Darier and White, of Boston, have described similar Protozoa as being the essential cause of a rare form of skin disease, which has been named "keratosis follicularis" or "psorospermosis folliculaire végétante."

