SCIENCE

VOL. LXI JUNE 12, 1925 NO. 1589

CONTENTS

Some Newer Aspects of Cancer Research: DR. ERWIN F. SMITH 595

Dinosaur Feed: PROFESSOR G. R. WIELAND 601

Scientific Events:

Robert Simpson Woodward; Lister Memorial Lecture; The Seismological Society of America; Transfer of the Bureau of Mines to the Department of Commerce; Fellowships Awarded by the John Simon Guggenheim Memorial Foundation; Institute for Biological Research at the Johns Hopkins University 603

Scientific Notes and News 606

University and Educational Notes 609

Discussion and Correspondence:

The Laboratory Method in the Teaching of Botany: DR. CHARLES W. ELIOT. *The Method of Science:* EDWARD H. DAVIS. *Weather Conditions at Sumatra:* DR. C. BRAAK and DR. C. G. ABBOT. *Calendar Reform:* ALVAN L. DAVIS. *The Gilboa Fossil Forest:* THADDEUS MERRIMAN 609

Scientific Books:

Cushing's Life of Sir William Osler: DR. F. H. GARRISON 611

Special Articles:

On the X-Ray Diffraction Effects from Solid Fatty Acids: DR. RALPH W. G. WYCKOFF, DR. FRANKLIN L. HUNT and DR. HERBERT E. MERWIN 613

The American Society of Mammalogists: A. BRAZIER HOWELL 615

The American Mathematical Society: PROFESSOR ARNOLD DRESDEN 615

Conference of Apparatus Makers and Users: PROFESSOR F. K. RICHTMYER 616

Science News x

SCIENCE: A Weekly Journal devoted to the Advancement of Science, edited by J. McKeen Cattell and published every Friday by

THE SCIENCE PRESS

Lancaster, Pa. Garrison, N. Y.

New York City: Grand Central Terminal.

Annual Subscription, $6.00. Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the association may be secured from the office of the permanent secretary, in the Smithsonian Institution Building, Washington, D. C.

Entered as second-class matter July 18, 1923, at the Post Office at Lancaster, Pa., under the Act of March 8, 1879.

SOME NEWER ASPECTS OF CANCER RESEARCH[1]

HAVING spent a good part of the last eight months in Europe among cancer men it appears to me worth while to set down in simple words a few of the things I have seen and heard. What I have to say concerns diagnosis, treatment, biology and causation.

DIAGNOSIS

Diagnosis is easy when the tumor is superficial, but difficult when the tumor is internal, and especially difficult in early stages of growth; yet it is in just these stages that cancer is most amenable to surgery. Any aid, therefore, that the biologist can give to the surgeon is all important for the patient.

Two methods of early diagnosis are now coming into prominence in Europe.

Kotzareff and Weyl, of Geneva, have discovered that if radio-colloidal substances are injected into a cancerous patient there is a selective fixation of the radium in the rapidly multiplying cancer cells. If now a sensitive photographic plate be exposed over the suspected part for some hours, the outline of the tumor is visible on the plate when it is developed. Dr. Kotzareff now at the École medicale in Paris showed me very interesting photographic plates demonstrating this. The only other tissues giving the same or a similar reaction are young embryonic tissues. At present the exact composition of the radium colloidal substances is a secret known only to Mr. Weyl. They are said to be administered in such dilution as to be entirely harmless to man and the experimental animals, a few millicuries only, in serum derived from the patient. More work needs to be done so that the exact composition of these substances may be known generally and the limits of usefulness of the method determined. Dr. Kotzareff needs support for his work and would like to come to the United States.

The other method of early diagnosis is a serum method discovered and perfected by Dr. Botelho, chief of the cancer laboratory of the surgical clinic of Dr. Hartmann in the Hotel Dieu, the great hospital near Notre Dame in Paris, a method on which he has been at work for half a dozen years. It con-

[1] Opening address of the president at the eighteenth annual meeting of the American Association for Cancer Research, Navy Medical School, Washington, D. C., on May 4, 1925.

sists in adding to centrifuged suspect blood serum dilute nitric acid and an iodine reagent in several small doses at short intervals and shaking in a test tube after each addition. Normal serum and that from non-cancerous patients remains clear after the final treatment. That from cancerous patients remains persistently clouded. To obtain the full effect of this reaction all the serums must be reduced or increased to a norm of specific gravity (8 per cent. albumen) as determined on the spectroscope, the dense ones by dilution, the dilute ones by concentration for a short period in the blood temperature oven. When this is done, he tells me, all the normal serums remain clear and all the cancer serums remain clouded. Dr. Botelho was good enough to show me his MS literature and to demonstrate his method for me. Dr. Itchikawa, whom I met in Paris, told me he had tried it on tar cancer of rabbits with confirmatory results.

TREATMENT

Early surgery remains the best treatment for cancer, but radium and X-ray are useful palliatives; and, in case of many superficial cancers, they appear to offer also good chances of long-delayed new growth, if not of permanent cure. It is perhaps too early to speak positively about the latter, the methods are so new, but in various localities some patients have remained well for periods of five years and more following treatment and many for periods of two and three years. In another ten years we shall be able to judge much better of their relative effectiveness in comparison with surgery. At the Madame Curie radium laboratories in Paris Professor Régaud and his associates showed me many interesting things, including numerous photographs of remarkable cures effected, some by X-ray, others by radium. They are there studying intensively the best methods of application, and, on experimental animals, the best dosage. Both radium and X-ray are deadly weapons in the hands of the incompetent. About 500 selected cancer patients pass through their clinics each year, and I was told that 75 to 80 per cent. are cured, but their full records go back only a few years! Prof. Régaud is considered to be the most expert radiologist in France. He is also famous for his studies of mitochondria in animal cells. I saw similar encouraging results two years ago at a clinic in Buffalo at the State Institution for Malignant Disease. Twenty or thirty persons treated by X-ray, one to five years previously, for cancer of the breast, cervix, face, etc., were examined critically by visiting surgeons, who pronounced them to be free from the disease, so far as a physical examination could determine.

PALLIATIVES

Radium and X-ray may also be used as palliatives in the hopeless cases, reducing the pain and the odor.

Dr. Botelho in Paris is also treating inoperable cancer of the face and breast with absorbent cotton compresses wet every ten minutes in a mixture of physiological salt solution and glycerine, to which purified tannin, potassium iodide and iodine are added. These compresses are kept on several hours running, night and morning. The cancerous tissue sloughs, all odor disappears, and the normal tissues are not injured. The mode of action appears to be by the formation of precipitates and the constriction or obliteration of blood vessels. I saw one desperate case of breast cancer in which the intense pain had been relieved and the rapid progress of the disease checked. I also saw a letter from this woman's husband expressing the utmost gratitude for her improvement. Up to this time the method has been tried on only a few cases, but on these with very surprising results.

BIOLOGY

In recent years there have been two camps of oncologists, the one believing malignant tumors to be of non-parasitic origin, and the other, a very small minority, of which I have been one, believing that the method of growth in cancer points unmistakably to a parasitic origin. The former have believed the cancer cell to be, so to speak, a normal cell with the brakes taken off, the latter that the cancer cell must be, chemically and physically, an abnormal cell, the driving power of which is some extraneous influence more powerful than the physiological control which normally keeps all the organs and tissues of the body in harmonious cooperation.

If the cancer cells are physically and chemically unlike normal cells it should be possible to demonstrate it experimentally and this has now become an accomplished fact.

Dr. Otto Warburg, of Berlin, has shown by very ingenious and exact methods of experimentation that if grape sugar is present the cancer cells can live anaerobically for a considerable period. Owing to splitting of the sugar during this anaerobic growth, there is an excess of acid produced in cancerous tissues. Normal tissues of animals also produce an excess of acid when they are grown anaerobically, but this acid, said to be lactic acid, they are able to destroy under aerobic conditions so that it can not be found at all, whereas the cancer cells can not do this. In them it remains as an irritant. He thinks, as I do, that the cancer cell not only behaves unlike a normal cell but also contains unlike substances. To a weighed small amount of dry tumor tissue he

adds sodium bicarbonate in serum and from the amount of CO_2 liberated calculates the amount of acid present.

Using the Flexner-Jobling rat carcinoma Warburg has found that, when grown anaerobically in presence of grape sugar, the tumor tissue by glycolysis produces its own weight of lactic acid every eight hours. In a given time, he says, the tumor produces one hundred times more lactic acid than blood, two hundred times more than quiescent frog muscle, and eight times more than active muscle. Tumor sections in sterile Ringer's solution (a physiological salt solution) at body temperature continue to split sugar for days, yet, if such sections are taken after three days and introduced into rats, they give as many cancer takes as fresh tumors. The carcinoma tissue, in other words, behaves like a yeast. If now the tumor tissue be grown aerobically the glycolysis is somewhat reduced, but does not disappear, the respiration of the carcinoma cells being too limited. Embryonic tissue, on the other hand, grown under aerobic conditions in the presence of grape sugar forms practically no lactic acid, its respiration being sufficient to eliminate glycolysis. The metabolism of rat carcinoma tissue in presence of oxygen is, therefore, a mixture of oxidation phenomena and anaerobic splitting, and preponderantly it is the latter, in about the ratio of one molecule of sugar oxidized to twelve molecules split. The epithelium of human carcinoma, grown anaerobically in presence of grape sugar, behaves in the same way, producing each hour about 16 per cent. of its own weight of lactic acid.

"These experiments show *what* happens when a carcinoma arises, but not *why* it happens."

Wir haben uns im Laufe unserer Arbeit die Frage nach den wirkenden Ursachen oft gestellt, und immer wieder hat sich der Gedanke aufgedrängt, dass der "Reiz" bei der Entstehung der Carcinome nichts anderes ist als Sauerstoffmangel.

Warburg suggests that normal resting epithelium is a mosaic in which a few cells are strongly glycolytic, while most are oxidizing cells, and that when for any reason (pressure, sclerosis of vessels, presence of bacteria, etc.) there is a lack of oxygen the nonglycolysing cells perish and the others grow. I was told by Dr. Carl Posener, who demonstrated for me, that sarcoma behaves the same as carcinoma. He said that they had made many tests and that the acid is practically all lactic acid, but I suspect, as does also Waterman, that small quantities of other acids may be present and act as stimulants to cell-division.

Waterman, of Amsterdam, has verified Warburg's results obtained on rats, *i.e.*, the glycolytic action of cancerous tissue on grape sugar with production of a great excess of lactic acid, using, in vitro, a variety of human cancers.

Dr. Russell of London (recently deceased) has also published some data indicating that cancerous tissue (he used that of mice) is able to assimilate certain carbon compounds (some of the pentoses) which normal tissues can not assimilate. If this proves to be correct, here is another way in which tumor cells differ from normal cells.

Some years ago Clowes pointed out that the electric conductivity of tumor tissue differs from that of normal tissue. This has been confirmed by Waterman in Amsterdam and by others. Other differences will be mentioned later when I take up the Copenhagen work.

Five years ago in my text-book on "Bacterial Diseases of Plants" (Saunders, 1920, Philadelphia and London) I propounded the theory that oxygen-hunger is the cause of the abnormal growth in tumor tissue, the rapidity of the cell division depending on the degree of the hunger. The cell breathes through its entire surface and the smaller the cell the greater the respiratory surface, in comparison with the amount of protoplasm to be aerated. It seemed to me under the conditions offered by the crowngall, *i.e.*, presence in the tissues of a parasite producing acid and alkali as the result of its growth, that the cell-respiration must be very thoroughly upset and as a consequence that the tumor cells *must* divide or be asphyxiated. The tissue of the tumor plays a losing game, but it does the best it can under adverse circumstances. I had many observations and experiments that seemed to me to support such a view, but no absolutely conclusive evidence. This we now have, I believe, in Otto Warburg's work. What I advanced partly on experimental, partly on theoretical grounds, he seems to have established experimentally beyond reasonable doubt. If he is right, oxygen-hunger explains the abnormal cell multiplication in tumors.

What leads to oxygen-hunger? According to my hypothesis it was disturbed respiration due to extraneous substances (acids and alkali) thrown into the tissues as the by-products of parasites. These must very effectually upset normal conditions. I conceived the next step to be paralysis or partial paralysis of the surface layer of the protoplasm, the ectoplasm governing outflow and intake, leading to loss of solutes and to an excessive intake of water followed by repeated cell division. However we explain it, the first stage in crowngall, what we may call the precancerous stage, is a decided enlargement

of the cells followed by rapid cell division. This resembles what occurs in animal cancer, as Deelman in Holland has shown conclusively for early stages of tar-cancer in the skin of the mouse. I have examined several hundred of his slides and I am convinced that he is right. If we may believe various reputable workers, the same thing occurs in human cancer. I have summarized some of these opinions in *Journal Cancer Research,* Vol. VII, No. 1, January, 1922.

I believed the excess of acid and alkali produced in flask cultures in the presence of grape sugar by the crowngall organism (*Bacterium tumefaciens*) must also be produced in excess in the tissues of the plant where grape sugar also occurs. This we now know to be the case from our potentiometer studies. In fact, there may be twice as much acid in crowngall tissues as in normal young tissues, tested under like conditions—acid or acids that can not be demonstrated in millivolts interpretable as pH, but which are demonstrable by electrometric titration with sodium hydroxide, *i.e.*, acids locked up in the tissues in the form of salts of ammonia (a substance produced by the parasite in flask cultures and undoubtedly also in the tumors). This coincides very well with Dr. Warburg's findings of an excess of acid in animal cancer cells, only, in crowngall, the acid appears to be produced by the parasite, whereas in the rat-cancer no parasite has been demonstrated, although I believe one exists.

It does not follow from what I have said that the *volume* of respiration of tumors would be greater than that of normal tissues, bulk for bulk, but only that the effort would be greater, as indicated by rapid cell division. As a matter of fact, Warburg has found the respiration in the Flexner-Jobling rat carcinoma to be less than in the normal tissues.

Following the amazing results of tar paintings on the skin of rabbits and mice in recent years, the general trend of medical opinion has been to the belief that cancer is to be explained wholly as the result of chronic irritation, *i.e.*, on Rudolph Virchow's theory. Personally, I believe the pendulum has swung too far in that direction.

Dr. Fridthof Bang, in Copenhagen, has observed cancer in the nose of a man following a single splash of hot tar. He has also produced two cases of skin cancer in mice, slides of which I have seen, by a single burning with the electric cautery. One of these cases developed immediately and the other after one and a half years. In a third mouse he obtained a receding cancer. These observations and experiments lead Bang to believe that Virchow's irritation theory, *i.e.*, the continual long application of irritants to a definite spot, is not the direct cause of cancer. Findlay, in London, has also produced skin cancer in three mice by a single application of hot tar (*The Lancet,* April 4, 1925). I talked with Dr. Findlay, but did not see his slides. He is associated with Dr. Murray, of the Imperial Cancer Research Laboratories in London, and I have full confidence in his work. Dr. Masson, cancer specialist in Strasbourg, showed me slides of a cancer of the thumb which developed two weeks after a man stuck a splinter in his hand, and I heard of a somewhat similar case at the Middlesex Hospital in London, but did not see the protocol. My impression, from what I was told by Dr. Chambers, is that this was in a young person but appeared some time after the reception of the wound.

Dr. Albert Fischer, of Copenhagen, an intensive student of cancer, who formerly worked with Dr. Carrel, has learned how to grow the cells of the Rous' chicken sarcoma out of the body in a pure culture on slides in drops of serum from chicks with a trace of fresh embryo juice added, and from such cultures he has obtained numerous virulent infections, some of which I saw. He has accomplished this by adding a bit of muscle to the serum. The sarcoma cells invade the muscle and destroy it and liquefy the serum, something normal tissues can not do, so that here seem to be other ways in which cancer cells differ from normal cells. In this manner outside of the chicken he has carried along the cell cultures for a period of two years and the last transfers (some of which I examined under the microscope), when introduced into chickens, are as virulent as the cells taken directly from the tumor. This tumor metastasizes so freely and so extensively in vital organs, *e.g.*, the heart wall and the lungs, that it seems impossible a chicken could live so long, riddled with tumors. The work of carrying on the cell-cultures is herculean, since they must be transferred to fresh serum with muscle every second day. He tells me also that a single sarcoma cell will multiply in a culture and invade and destroy the fragment of muscle in a few days, whereas the muscle itself does not grow at all, nor will single fibroblasts grow.

ETIOLOGY

We come now to the causation of cancer, and I will begin with Dr. Rous's chicken sarcoma. It is too late in the day, I think, to deny that this is a malignant tumor, a true sarcoma. All with whom I have talked, *i.e.*, those who have done much work with it, are agreed that it is a true tumor. It will be remembered that the beautiful researches of Dr. Rous proved conclusively that this malignant tumor is due to a filterable virus, that is, to something separable from the tumor tissues and that in consequence the

popular slogan, "the cancer cell is the only parasite," was no longer available to obscure research. It seemed that the "virus" of this tumor must be a living thing, but in spite of enormous labors Dr. Rous was unable to see it or to cultivate it.

Dr. Gye, of the National Institute for Medical Research in London, a student of cancer, of serums and of vaccines, for fifteen years, and for the last two or three years intensely interested in the Rous' chicken sarcoma, has been able to cultivate the "virus" and multiply it in test tubes exactly as we do a living thing, and that, too, through a whole series of tubes of fluid media, and from the final tubes (7th to 9th transfer) he has obtained numerous striking infections in chickens (more than 40). His method is to put 0.02 of a cubic millimeter of the virus into 5 cc of his culture medium, incubate it for three days, then transfer a similar quantity of the fluid to a second tube, incubate that for three days, and so on. The final dilution of the original material, if it were merely a chemical substance, is so great as to be harmless, and the virulence (the active tumor-producing power) in the end term of the series can not be due to a diluted chemical but must be due to a living multiplying organism. Any other explanation is unthinkable.[2] There is, however, no pellicle, precipitate or clouding in these fluid cultures, so far as I could see, nor is anything visible under the highest powers of the microscope; nevertheless, the organism is there, *in a particulate form.* This Dr. Gye has demonstrated by means of the centrifuge. If fluid containing the virus is whirled 9,000 revolutions per minute, and certain other necessary conditions are properly adjusted (I am not at liberty to state what they are), all the virus is thrown down to the bottom of the tube and remains virulent, whereas the previously infectious supernatant fluid has now become harmless as water, but even in the precipitate no organism is to be seen, stained or unstained, by use of the ordinary microscopes. Dr. Gye has also observed another interesting thing, *viz.,* when his cultures become contaminated with cocci and other microorganisms they cease to be virulent. There seems to be an antagonism. He formerly believed malignant tumors non-parasitic, but now he believes very firmly that all or most of them are of parasitic origin. He is full of enthusiasm and believes, as I do, that the solution of the cancer problem is not far off.

[2] Allard has shown for tobacco mosaic and Doolittle for cucumber mosaic that the juice is only rarely infectious much beyond dilutions of 1 to 10,000, as Olitsky has also shown, and such dilutions are surpassed in the second tube of Dr. Gye's series, whereas in his seventh tube in series the dilution is in the trillions and in his ninth tube it is in the quadrillions.

It remained for the physicist, Dr. Barnard, a colleague of Dr. Gye, to demonstrate the organism, using special objectives and monochromatic light. I have been in his laboratory and have seen the body dancing about in the culture fluid (rabbit serum) and also mounted slides of it and photomicrographs of it. It is the same type of germ as the pleuropneumonia organism, but smaller. The latter, seen first by a Frenchman, was described as resembling a yeast, but seen by the subdued monochromatic green-band light of a mercury lamp and with Dr. Barnard's objective of 1.3 aperture, with which he can see down to 0.1 μ, it has none of the characters of a yeast or of an ordinary Schizomycete.

The general method of development of these two organisms, as worked out by Dr. Barnard during the last two years, is to begin as small glistening particles (I saw them under a magnification of 1,800 diameters). These apparently swell up into soap-bubble-like, tiny globes, at least all sizes and gradations of such bodies appear in the fluid. Then, in the surface film, never in the interior, slight thickenings appear, here and there. These thickenings, of which there may be several on a sphere (I saw as many as six or eight on some of the spheres), finally round off, push out into the fluid, remain attached for some time to the periphery of the sphere by a narrow pedicle and then become free, as glistening points, to go through a similar swelling and evolution. I saw nothing resembling a nucleus or a protoplasmic content in any of these bodies.

It would seem to me also from Dr. Gye's work, which is unpublished as yet, that he must have attenuation of the virus in some of his tubes *and a vaccine,* but we must wait for the completion of his studies to know definitely as to this. I saw nothing in Europe more interesting than his work and that of his colleague. More money is urgently needed there for research assistants, and, in my opinion, it could be nowhere expended more wisely. It should be forthcoming abundantly and at once, while these two remarkable men are living and active.

It seemed to me immediately that this work might also throw light on the origin of some of the mosaic diseases of plants, in the cells of which various peculiar and problematic bodies have been observed. I did not then know of Dr. Olitsky's work at the Rockefeller Institute for Medical Research in New York. His studies (*The Jour. of Exp. Medicine,* January 1, 1925) seem to demonstrate that in tobacco and tomato mosaic there is also a particulate multiplying organism and not, as Beyerinck suspected, a fluid contagium, whatever that may mean. I was never able to formulate a clear idea as to what Dr. Beyerinck's "contagium vivum fluidum" could be, but always I

believed and said that the virus of tobacco mosaic would surely turn out to be a microorganism. Olitsky has done for the tobacco mosaic exactly what Gye has done for the chicken sarcoma, and the etiology of mosaic diseases is now in a fair way to be resolved into the presence of parasites in the tissues, just as the logic of the phenomena all along required it to be! Probably with Dr. Barnard's apparatus the organism of the tobacco mosaic can be seen and photographed. It would be worth a journey to London to determine this.

I come now to the work of Dr. Ferdinand Blumenthal and his assistants, Dr. Hans Auler and Miss Paula Meyer, in Berlin. Dr. Blumenthal is the director of the cancer laboratory of the great Charity Hospital on Luisen Strasse and the responsible editor of the *Zeitschrift für Krebsforschung,* the leading cancer journal of the world.

After several years of work they reported that they had been able to obtain from human breast cancers a bacterium in pure culture resembling culturally *Bact. tumefaciens,* the cause of crowngall in plants, and with this organism had been able to cause malignant transplantable tumors in rats and crowngalls in plants. These statements were so surprising and interesting that I went to Berlin and spent about two weeks in their laboratory at the Charity Hospital in order to see as much as possible of their work and to clear up certain doubts raised by the reading of their papers. I was received very courteously. I asked a great many questions and was shown cultures, slides and inoculated plants and animals. Much of my scepticism disappeared on learning exactly how things were done. It is not always possible for a good experimenter to write up his results in a convincing way. That is a special gift. Some of their statements should have been more explicit. I thought I saw various doubtful things in the papers. I was prepared to believe that the rat tumors were accidents, but after being on the ground the only conclusion I could come to was either that the organism from the human cancer is the cause of the rat tumors or else that they are due to some invisible virus introduced along with the heated oedematous cancerous breast serum which was added to the bacterial culture along with the kieselgur (diatomaceous earth) as a second irritant. As for the plant tumors, the organism *PM,* which looks much like the crowngall organism on agar streaks, and is said to behave the same serologically (cross agglutination tests in rabbit serum), not only produced good typical looking crowngalls on sunflowers and other plants two years ago, but is still able to do so. I saw them and brought away specimens and also some of the rats and stained sections of the rat tumors. I counted thirty-two metastases in the lungs of one transplant rat inoculated with *L,* and I have here a rat inoculated with *PM* showing five conspicuous secondary tumors.

Hearing that the Berlin experiments had been repeated in the Aktien Gesellschaft Serum Laboratory Dresden, with the same results, and that an address was to be given on the subject before the Dresden Medical Society, I went down there, heard the address, saw the experiments, talked with the experimenter, Dr. Reichert, and with the director of the laboratory, Dr. Behlke, and most of his associate pathologists. They have done two things in Dresden. They have propagated the tumor *PM* through a long series of rats starting from an implanted rat received from Dr. Blumenthal and they have originated new tumors. I saw a dozen or more of the dissected rats full of secondary tumors. There can be no doubt as to the malignancy of the tumor, and to call it an infectious granuloma does not help matters. It looks to me like a carcinoma. The second thing they have done removes one of my objections to the Berlin work, *viz.,* use of cancer serum as an irritant. Using cultures of *PM* (obtained it will be remembered two years ago from an inoperable human breast cancer) they have produced in rats two metastasizing, malignant, transplantable tumors without the addition of any cancer serum. These had been carried to the fifth and sixth generation of transplants when I was there early in March. The percentage is low, it is true, two cases only out of fifty rats inoculated (the tumors receded in the others), but then we must remember that the organism is in a strange host, and that rats are often resistant to their own tumors. Up to the time of my visit no efforts had been made in Berlin to obtain by breeding a race of rats more susceptible to the bacterial inoculations, but now they will try to do this, at least they promised to undertake it. Dr. Schmorl, the well-known pathologist, in discussion of the Dresden paper, said the structure of the tumor left him in some doubt. He thought the tumor might be carcinoma because so far it has never been found in the spleen (Miltz), whereas the commonest rat-tumor, the rat-sarcoma, is often found there. The tumor is unlike any other rat tumor I have ever seen. The Dresden tumors are like the Berlin ones, and it seems to me very improbable that they should be, all of them, accidental tumors, and yet all of the same peculiar type. The tumor is a diffuse, rather non-typical looking carcinoma, as if it might be a carcinoma plus a bacterial infection, yet in some of the metastases it is a sarcoma. This is not surprising, however, as often in tar-cancer in mice sarcoma and carcinoma appear in the same animal. Dr. Fibiger, of Copenhagen, showed me two metastatic nodules in the lung of a mouse (almost in the same field of the microscope), one a typical sar-

coma and the other an equally typical carcinoma. Polymorphs are numerous, and I think I have made out bacteria in places, but these often occur in rat-tumor transplants. As I have said, the hypothesis that they are pure accidents appears to me untenable and the Dresden work reduces me to one of two alternatives. Either the rat tumors are due to the bacterial culture *PM* or else to some invisible virus attached to the culture and carried along with it. In either event it suggests parasitism. Just as I left Berlin I saw a third rat tumor (good primary, size of the end of my finger, with liver metastasis) produced from a third human breast carcinoma. This is *Beta*. It was just being transplanted, and I have not heard whether the transplants have grown. I showed the rat slides to Jensen in Copenhagen. He said he had never seen any tumor like it. One he pronounced a sarcoma, another from the same rat "possibly an endothelioma."

I found general scepticism in Berlin and in other parts of Europe as to the value of Dr. Blumenthal's work, but it is well to remember that the attitude of medicine toward any startling new discovery has been always one of rank scepticism, which in many cases is only another name for mental inertia. I have learned, therefore, to discount all criticisms which are not based on good opposing work. There are also many jealousies and much misinformation. The cancer laboratory at the Charity Hospital is poor and has urgent need of money for assistants and for additional animals and animal houses. Just now it would be a good place to put money, hoping for interesting definite returns. A few thousand dollars would be of great service and many a rich man who will die of cancer would not miss it in the least and might render a real service to humanity, just as he might also by giving money to the American Association for Cancer Research.

It is the more interesting that Dr. Blumenthal should have reached the conclusion that the crowngall organism is the type of a whole group of cancer parasites, since originally he shared and expressed the opinion of all German pathologists that the American crowngall studies were of no importance whatever to cancer research and only changed his opinion after studying and experimenting with the plant tumor for half a dozen years.

Professor Gosset, the great surgeon of the Salpêtrière in Paris, has also established a laboratory for the study of crowngall and has put Dr. Magrou, a Pasteur Institute man, in charge of it. Dr. Borrel, in Strasbourg, is also now studying it and a great variety of other tumors very actively and has a superb collection of cancer slides. There also a large amount of research is going on upon tuberculosis, syphilis, vaccine virus and all sorts of human and animal diseases. Dr. Borrel has found the cornea of rabbits an excellent place for the propagation of vaccine virus and here by staining methods he had demonstrated the presence of great numbers of cocci, sharply stained (I saw them under the microscope) and closely resembling the bodies he has found in *Molluscum contagiosum*, but from neither disease can they be cultivated. I was much impressed by what I saw in the Strasbourg Medical School. There I was received very courteously and invited to give two lectures to the fourth-year medical students on plant tumors.

Personally, I never thought the crowngall organism could be the cause of cancer in man, but only that cancer might be due to some parasite endowed with similar chemical activities. My reason for disbelief was that, in those strains of the organism which I tested in the thermostat, growth ceased a little under human blood temperature, but always in the back of my thought was the idea that there might be strains of the organism able to grow at 38° C. and for this reason I generally handled the tumors carefully and often sterilized my hands afterward. It was on my mind also to try to educate our strains of the organism to grow at higher temperatures than 36.5° C., but I never found time to try it. I will now try to discover strains able to grow at 38° C.

Looking over the whole field of cancer research I can not resist the feeling that great progress is being made and that the time is not far distant, and perhaps within our own generation, when we shall not only know the cause of human sarcoma and carcinoma, but shall have much better methods of treatment and especially of prevention than any now available. A vaccine is what I hope for and a carrier that may be destroyed, possibly also, a bacterial antagonist. As Pasteur said very often, "The essential thing is to repeat our experiments and not to be discouraged."

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DINOSAUR FEED

THE idea that dicotyls arose suddenly about the time smaller mammals appeared and the plant-eating dinosaurs reached maximum size and widest distribution, has led to some quite unimaginative speculation as to ancient reptilian food habits. With Jurassic hillsides so dominantly clothed in araucarians, pines, ginkgos, cycads and ferns, and lowlands beset by scouring rushes and stoneworts, the food of the great browsing animals seemed limited. Zoopaleontologists suggested, for instance, that terrestrial ortho-