The Bradshaw lecture on cancer : delivered at the Royal College of Surgeons of England, on Wednesday, Decmber 7th, 1910 / by Sir Alfred Pearce Gould.

THE BRADSHAW LECTURE ON CANCER.

The Bradshaw Lecture on Cancer

Delivered at
The Royal College of Surgeons of England,
on Wednesday, December 7th, 1910

BY

SIR ALFRED PEARCE GOULD, K.C.V.O.,

M.S.Lond., F.R.C.S.Eng.,
Senior Surgeon to the Middlesex Hospital

London
JOHN BALE, SONS & DANIELSSON, LTD.
OXFORD HOUSE
83-91, GREAT TITCHFIELD STREET, OXFORD STREET, W.

I AM indebted to Dr. Bashford, the Director of the Imperial Cancer Fund Laboratory, for the illustrations which accompany this lecture.

The X-ray treatment of the patients mentioned on pp. 70-75, was carried out under the supervision of my colleague, Mr. Cecil Lyster.

THE BRADSHAW LECTURE
ON
CANCER.

In 1884 the late Sir William Savory discussed in the third Bradshaw lecture the Pathology of Cancer. He pronounced the cancer cell to be an "embryonic" or "rudimentary" form of cell, possessing great powers of multiplication and of endurance, but differing from true embryonic cells in its lack of power of differentiation. And then he used these interesting words:—

"And while tumours of the most innocent type touch, and indeed pass into, natural structures, the most malignant touch, if they do not actually pass into, the class of parasites. . . . . The interval between the worst kind of cancer and a parasite must be a very narrow one."

He suggested that the failure of the

experiments in cancer grafting was probably due to the "crude conditions under which they had been performed." He concluded thus :—

"Before we shall ever be able to answer the question, Why or how do tumours form? it seems to me we must be able to solve the problem of normal growth and development, and to answer the question why or how it is that these continue up to a certain point and then suddenly cease."

For the succeeding nineteen years the Bradshaw Lecturers dealt with other subjects, but in 1903 Sir Henry Morris gave a learned review of the many theories that had been advanced to explain the origin and nature of cancer. He specially discussed two theories, the microbic or parasitic theory, which he held to be "non-proven," and Cohnheim's theory of "cancer matrices," ante-natal and post-natal. This theory he strongly supported as explaining all the facts of the disease then known, and he confidently foretold for it a speedy acceptance by all pathologists.

Two years later, in 1905, you, Mr. President, announced, as the title of your Bradshaw lecture, "Carcinoma is a Parasitic Disease," and stated :—

"That the carcinoma cell is an independent organism, like many a protozoon ; that it lives a life which is wholly independent and proper to itself ; and that it lives as a parasite in the body of the animal which is affected with carcinoma, deriving its nourishment from the host, and having nothing to pay the host for the sustenance of which it robs him."

It is needless to say that each of these divergent theories has been discussed from the standpoint of a very wide and accurate knowledge of the subject, and that each in turn has been supported with extraordinary ability and with the enthusiasm of a strong personal belief. For me to attempt another review of the same facts and arguments would be to act the disastrous part of Phaeton, and yet I propose, Sir, to raise once again the great problem of the nature of cancer, not because I can read aright the riddle solved so differently, and with such mutual

destructiveness, by my predecessors, but because within the last few years the workers in our cancer laboratories have added so much to our store of knowledge that it seems wise to see how far the new facts support or refute former conclusions. We are like children putting together a dissected picture: we slowly look over and often vainly try to fit together the irregular pieces of the puzzle, but gradually order comes here and there out of chaos, and as piece after piece finds its proper setting, the picture grows until the fitting in of the final fragment reveals the whole design.

In addition to the influence of the general progress of biological knowledge, two discoveries have caused a great development in cancer research: the proof that cancer can be transferred from animal to animal, and the demonstration of the influence of radio-active bodies upon cell growth. Scientific workers have devoted themselves to the solution of the problem of cancer with new courage and more confident hope since they saw that it could be submitted to that experimental

method which has so often dissipated the darkness of ignorance. All over the civilized world cancer research laboratories, more or less exclusively devoted to this quest, have been founded, and never before have the efforts of scientific men been so largely centred in the study of any one disease. Highly gifted investigators are devoting themselves with praiseworthy devotion to the study of the internal structure and arrangement of cancer cells, to a search for the forms and evidences of the presence of an invading organism, to a close scrutiny of all that takes place in the artificial transmission of the disease from animal to animal, and to the investigation of the various abstruse problems in bio-chemistry and physics that it is hoped may aid in the discovery of the nature and cause of cancer. This College, in conjunction with our sister in Pall Mall, by the initiation, control, and housing of the Imperial Cancer Fund, has taken a very prominent part in this movement, and it is a matter of great satisfaction that the researches carried out in our laboratory are univer-

sally recognized as having been of fundamental importance. We gladly recognize that all the success which has attended, and may hereafter attend, the labours of Dr. Bashford and his distinguished associates is not due to the association with these Royal Colleges, nor to the sources from which the Fund has been collected, but to the ability, the wide knowledge, the patience, and the honesty that are associated with the laborious industry of the workers. It is not my purpose to give a detailed account of the latest results of cancer research, but rather briefly to enumerate some of them, and to see whether, and how far, they enable us to unravel what has hitherto been a tangled skein.

It is now known that *cancer occurs in all races of men.* Wherever adequate investigations have been made cancer has been found, and the fuller our knowledge of any people the ampler is the evidence of the presence of cancer among them. We are unable, therefore, to attribute the disease directly to the influence of race, of climate, of diet, of occupation,

of soil, of the subtler accidents of civilization, or to any of the associated and complex conditions that may be summarized as "environment." Not that these factors are without influence. Certain occupations are assuredly attended with peculiar liability to cancer; I need only mention chimney-sweepers and workers in X-rays, tar, and paraffin; and the beneficent effect of circumcision in greatly diminishing the incidence of epithelioma of the penis, and the pernicious influence of the use of the kangri, show us how the disease may be affected by social customs. It is clear, however, that we may not regard any of these conditions as the essential cause of cancer, for the disease occurs in their absence, and we must carefully guard against confusing subsidiary, accelerating, predisposing factors with the inevitable, constant cause of the disease.

Human statistics cannot be relied upon to substantiate or define the influence of race. Dr. Bashford has been at great pains to point out the imperfect character of our statistics of cancer incidence, and

he has clearly shown that the proportion of cancer reported among different nationalities is at present only a measure of the value of the material submitted to examination, and must not be taken as a true picture of the actual frequency of cancer. Only as care in diagnosis, in pathological examination, and in records improves and becomes uniform in all races of men shall we be able to state with precision what influence race, among many other factors, has upon the incidence of cancer. The experimental study of cancer has, however, shown that we must not assume that all races of men are equally liable to cancer. Very early in the investigations into the inoculability of mouse-cancer it was realized that there were serious discrepancies in the results obtained by different expert workers. Some of these discrepancies were caused by differences of technique, others by inattention to the age of the mice used for the experiments, and others again to the particular tumour experimented with. Chiefly owing to the work of Dr. Bashford these causes of variation in the

results obtained have been recognized and eliminated, and the influence of race has thereby been demonstrated. Such facts as these have come to light. Haaland found that a certain tumour grew on inoculation in nearly 100 per cent. of Berlin mice, in 24 per cent. only of Hamburg mice, and failed altogether to grow in Christiania mice. Loeb has a sarcoma which was readily propagated in white rats and could not be inoculated into coloured rats. Tyzzer has a carcinoma found in a Japanese waltzing mouse which he can transplant successfully in practically 100 per cent. of this particular family of mice, but which altogether fails to grow when inoculated into common mice. On the other hand, Jensen's tumour, which grows readily in common mice, cannot be inoculated with success into the Japanese waltzing mice. In hybrids, resulting from the crossing of common white mice and Japanese waltzing mice, the Japanese tumour grows as uniformly, and even more rapidly, than in the pure Japanese mice; but in the second and third generations of the off-

spring of these hybrids, the Japanese tumour cannot be inoculated at all. In his earliest inoculations of Jensen's tumour Bashford found it impossible to succeed with blue mice, while he obtained 25 per cent. of success with other tame mice. He also relates that a tumour sent to him by Dr. Michaelis, of Berlin, was transplanted into 19 Berlin mice, with the result that nine tumours grew; but only one small tumour developed in 182 tame London mice similarly inoculated. It is, of course, most important to keep clearly before one's mind the difference between the liability to occurrence of sporadic cancer in an individual or animal, and the susceptibility of such an individual or animal to the successful inoculation with cancer transferred from another. Such facts as I have just mentioned, however, make it imperative upon us, while recognizing the presence of cancer throughout the human family, to keep our minds open to receive a demonstration, should it come, of the influence of race apart from all other conditions upon the incidence of cancer.

Passing now from this first fact—that cancer is a disease of man wherever and however he lives—I would next remind you that we have recently learnt that *cancer is a disease that occurs in all vertebrate animals.* It is not limited to man, nor to man and primates, nor even to the great family of the mammalia ; it has been proved to occur in birds, reptiles, and fishes. The disease, as met with in the lower vertebrates, is not a similar disease, but veritable cancer, with the same histological characteristics and with those special biological features that we find in man—the uninterrupted growth, the power of infiltration, and the formation of metastases. The importance of this demonstration is enormous. It dissipates at once all those theories which find the cause of cancer in conditions peculiar to man, and we are forced to seek it in some influence which man shares with all other vertebrates. When we reflect that there is no known instance of an external infective agent or organism which spontaneously attacks and produces its characteristic pathological effects in all

vertebrata, or in all the varying physical conditions of environment in which cancer is found, the parasitic theory of cancer fails even to be a satisfactory "working hypothesis." We can only adopt it if the fact is demonstrated and Koch's conditions of proof are fulfilled; and such a demonstration is certainly not forthcoming.

That cancer can be transferred from host to host is now attested by thousands of successful experiments upon mice, rats, and dogs. Four facts have come to light during these inoculation experiments which are important to bear in mind. In the first place, the successful grafting of cancer from animal to animal is far more difficult to accomplish than is the inoculation of microbic disease. In the second place, it has been found that it is especially difficult to succeed in the primary grafting experiments of a sporadic mouse tumour into another mouse, or in the first graftings of a tumour upon a fresh family of mice. In the third place, as I have already mentioned, when allowance has been made for these variations the success of grafting experiments may vary consider-

ably in different races or families of mice. And then towering above these lesser facts is the greater, all-important one, that *cancer cannot be transferred to an animal of another species.* Cancer of a mouse is readily transferred to other mice, but it cannot be grafted upon a rat, or upon any other animal of another species. The same holds true of cancer of the rat and dog, and in this specificity of cancer we see the cause of failure of all experiments to graft the human disease upon lower animals. These failures were not due, as Savory suggested, to the "crude methods" employed, but to the working of a biological law.

The fact that an inoculable disease is specific in the sense that it cannot be transferred from species to species surely must be one of great importance in any consideration of its nature, for the grouping of animals into species is not artificial. The differences that we recognize between species have a greater element of permanence than those between varieties; the offspring of crossed varieties are fertile, while the hybrids of crossed species are

almost invariably infertile; the number of chromosomes in somatic cells differs widely, but it is constant for every species. Difficult, therefore, as it may be to express the distinguishing limitations of a species in terms which will satisfy the exacting criticisms of modern schools of biologists, all agree that the word connotes a reality, that it indicates an important step in the path of evolution, and that the limits between species are true landmarks. The enormously wide range of the incidence of cancer, the uniformity of its biological characters, and its specific inoculability are a triad of facts unique in pathology and of tremendous significance. Apart from many minor considerations, I venture to submit that they are inconsistent with what we know of infective or parasitic diseases. They, too, are no doubt "specific," but the specificity is attached to the disease, and neither to the animal nor to to the tissue in which it occurs. The tubercle bacillus leads to the same disease in the guinea-pig as in the man from whom the virus may have been taken. The minute anatomy of tubercle is the

same in whatever part or tissue of the body it arises; it does not vary with its primary site, as is constantly the case in cancer. Cancer is distinguished from all infective and parasitic diseases by the fact that the cellular parentage of a malignant growth is always definitely marked, and that whether it originates in squamous, columnar, or spheroidal epithelium, in endothelium, or in any of the forms of connective-tissue cells, it retains throughout its whole life, and whereever found, characteristic features of its parent cell. Parasitic diseases are anatomically and etiologically specific — specific in their structure and cause; cancer is specific not in structure, perhaps not in cause, but in the physiological characters of its cells.

The Cancer Cell.

The essential part of every cancerous growth is the living cancer cell. The cell, whether of carcinoma or sarcoma, is the one essential part, that which contains within itself all the potentialities of the whole of cancer. While it lives as a cell, the cancer is living; when it dies as a

cell, it is impossible to find or develop or excite any of the parts, or agencies, or faculties of a cancer. By no one has the demonstration of this fact been carried so far, or made so indubitable, as by Bashford and his fellow-workers in our laboratories. Their investigations into what takes place in the "early stages" of successful transference of a cancer from mouse to mouse have revealed that in the tiniest practicable graft all the introduced stroma and many of the centrally placed cancer cells die, but that the cells, or some of them, in the periphery of the graft live, do not undergo degenerative changes, and after a few days—usually about four—excite the formation from the fibroblasts of the host of a new supporting and vascular stroma, and themselves show the changes indicative of cell division. The parenchyma of the tumour, which ultimately may grow to a huge size, all develops directly from those cancer cells of the graft which were able to withstand the hurtful influences of the process of grafting. While it is possible to transfer cancer from mouse to mouse

so long as care is taken to introduce living cancer cells in the graft, it is impossible to do this when the cancer cells are destroyed by pounding in a mortar, or their vitality has been injured, as by the influence of heat. Indeed, Virchow's great doctrine of "*omnis cellula e cellula*" is peculiarly true of cancer. On the other hand, it has been equally clearly shown of inoculated infective granulomata that they grow not from the graft but from the connective tissue of the host. This difference between cancer and infective granulomata is of fundamental importance, a veritable *differentia*. The metastases of cancer and of granulomata may be alike in some of their coarser anatomical features, such as their site; but in their nature, in their true biological characters, they are absolutely distinct with a distinction which is vital and fundamental.

If the living cancer cell is the essential part of cancer, it is important to know what are its anatomical and physiological characteristics. A study of them demonstrates that the cancer cell is only a variation of a normal cell—it possesses neither

in structure nor in powers anything not found in the healthy cell. Let me rapidly mention the established facts about the living cancer cell.

First, *it possesses a great power of continuous multiplication.* So far as the experiments with Jensen's tumour have gone, it seems that the grafting can be carried out with it as successfully now after seven years as at first, and that from the small sporadic tumour in the mamma of a mouse a mass of cancer has been grown through an unknown number of mice, amounting to far more than a thousand times the bulk of the original tumour, or even of the original mouse. Bashford has particularly laid stress upon this striking fact, and has spoken of it as a "new" biological fact, but in that I think he has probably exceeded. Certainly in the protozoa such apparently endless multiplication and growth of living cells can be recognized. And when we cast our minds back to the development of the human ovum—a single cell — and remember that from it directly descends the entire mass of cells which form and

maintain through his three-score years and ten the full stature of a man, we see a power of cell growth which we need not shrink from comparing with that of a Jensen's cancer cell. But it is particularly noteworthy that in cancer this power of continuous multiplication is spontaneously manifested most often in the cells of an organism that has passed the period of youth and maturity, and has already entered upon the declining phase of life.

The second characteristic feature of the cancer cell is that *it retains the inherited limitations to type* of the cells among which it first appears. The descendants of an epiblastic cancer cell retain, in the main, the features of their early parent—a hypoblastic cancer cell bears its own family likeness, and the sarcoma cell is always a distinctively mesoblastic cell. Even in those remarkable experiences that have been so carefully studied and admirably recorded by Bashford and Haaland, when they observed in a series of transplantations of an undoubted epiblastic cancer of a mouse its gradual conversion, first into a cancer with a richly

cellular stroma, then into a "mixed" tumour, and finally into a sarcoma, it is clear that the mesoblastic cancer (sarcoma) thus formed sprang from the connective-tissue cells of the hosts, and that its cells are in no sense or degree the lineal descendants of the original cells of the epiblastic cancerous parenchyma. (See Plate I.)

Thirdly, *cancer cells develop and differentiate but little and irregularly.* Thus in a squamous epithelioma there is great variation in the extent to which keratinization of the cells occurs, and in some cancers we see such departures from type as a change from squamous to columnar cells and from spheroidal to columnar cells; the differentiation of a mammary cancer may be into acinous or glandular carcinoma, or into a combination of the two. (See Plate II.) This variation in growth has been best observed in the experimental work in laboratories, where the opportunities of studying the same strain of tumour in many succeeding stages of its growth and through many hosts afford scope for observation such as can never be found in human pathology.

PLATE I.—Diagrams illustrating the transformation of carcinoma into sarcoma.

FIG. A.—Carcinomatous tumour removed at a second operation, 3 weeks after the first operation ; at X, small areas of commencing sarcoma.

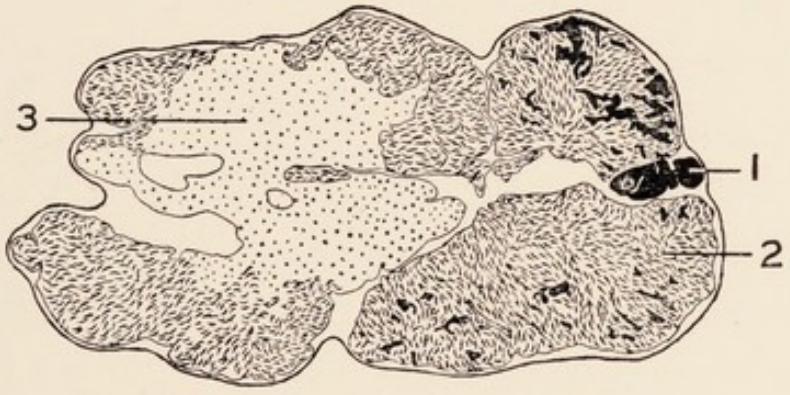


FIG. B.—The tumour removed 7 weeks later. The carcinoma (1) is almost wholly replaced by sarcoma (2). Necrotic tissue (3).

To face page 26.

The development of the cancer cell is neither purposeful nor effective. In glandular carcinoma no regular grouping of acini around primary ductlets is found, nor does the cell metabolism issue in useful secretion. In a squamous carcinoma no impermeable protective covering is formed, and in a sarcoma no useful fibrous bands or aponeuroses, no attached and functional muscles, no perfectly constructed and useful bone appear. In cancer there is cell multiplication in exaggerated degree, but a lack of adaptation to the many and varied needs of the organism. The cancer cell shows no new faculty or endowment, no power of "rising on its dead self"; it is a less highly endowed cell than its physiological parent.

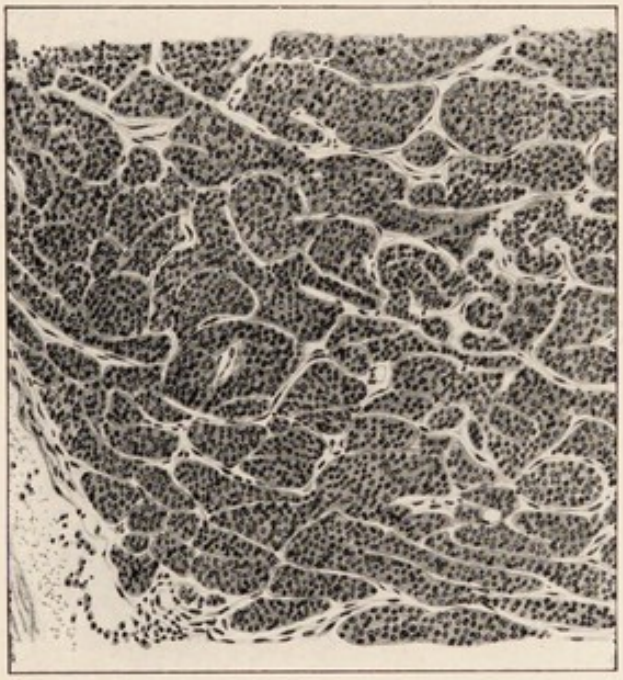
Then, again, *cancer cells exhibit periodicity in their growth.* Bashford has found that a mouse tumour has its period of active growth succeeded by one of less activity, and that the success of artificial transference of the disease to other mice rises and falls with this wave-like activity of the tumour, and he has found that this periodic activity is transmitted to the

tumours which arise from the grafts—that it is an inherent or inherited property. Similar variations in the rate of growth and activity of cancer are met with in the human subject, and we see periodic activity in metastases—periodic activity in their occurrence as well as in their growth. We must not look upon such variations as due, of necessity, to a change in the resisting forces of the patient; they are probably due to the inherent periodic growth of cancer. Physiological periodicity of cell growth is, of course, well recognized; I need only mention such examples as the sexual periodicity in animals, and especially in the human female, the periodic growth of young animals, the periodic growth of hair, the periodicity in the life-history of salmon, and the periodic variation in the colour of the fur and feathers of many mammals and birds.

The study of the form of cancer cells and the attempt to find in it some index of their nature have yielded but little that is positive. The many determined efforts to see within them foreign living forms,

PLATE II.—To illustrate the varying differentiation of successive generations of a Mammary Carcinoma of Mouse.

37/10$_2$K—11$_2$V.—Tumour of 10th generation (28 days). Pronounced adenomatous parenchyma. Stroma delicate. × $\frac{62}{1}$



37/60—7 R.—Recurrent tumour of 6th generation, 39 days after operation. Parenchyma alveolar, stroma delicate and scanty. × $\frac{62}{1}$

To face page 28.

whether of bacteria, of protozoa, or of yeasts, have failed. Bacteria may, of course, intrude within a cancer cell, but it was a cancer cell before the intrusion, and we may assert with some confidence to-day that there is no visible evidence of parasitism in the cancer cell. Nor has the hopeful and brilliant study of the mitoses of cancer by Walker, Moore, and Farmer, and their followers lifted the veil. It seemed that the theory that cancer was a gametoid tissue would explain much, or at any rate establish on a firm footing the nature of the disease. But we must regretfully consent to see that hope unfulfilled, and admit that mitosis is no key to the riddle.

Quite recently, however, it has been shown by Beckton that all the cells of man, except the keratin cells of squamous epithelium, the cells lining the collecting tubes of the kidney, the cells of unstriped muscle, and the unimpregnated ovum, contain certain granules, which are known as Altmann's granules. While unrecognizable in the protoplasm of the ovum, these granules are seen in the

unincubated blastoderm of the egg, and are readily recognized after six hours' incubation. Beckton has found them in mouse embryos of 8 mm. and 12 mm. in length, and in the rat embryo of 30 mm. They appear, therefore, very early indeed in the descendants of the original single ungranulated cell of the ovum. Beckton states that these particular granules are seen in the cells of the stroma of carcinoma, *but not in the cells of the parenchyma*, and while abundant in the protoplasm of inflammatory and granulomatous tissue they are invariably absent from the cells of sarcoma. Beckton examined also twenty-one mouse tumours sent him by Dr. Bashford, and in fourteen of them there were no granules, but in five instances they were present. They are therefore commoner in the mouse tumours than in the human malignant growths. Should further observation confirm Dr. Beckton, he will not only have given us a very useful method of diagnosis, but he will have established a morphological difference between cancer cells and most

normal cells. He will also have afforded an anatomical proof that cancer cells are not embryonic cells.

Of the *intracellular metabolism of the cancer cell* we know but little; it seems to beget no toxin, to generate no new substance, and to depart but little from the chemistry of health. And yet we cannot doubt that its special biological characters are inseparately linked with some intracellular chemical peculiarities. We have evidence of this furnished by some very careful spectroscopical observations made by Mr. Mottram in Dr. Lazarus-Barlow's laboratory, by which he has shown that the potassium content of the red corpuscles of cancerous patients is considerably higher than in health, the difference being represented by the figures 3 and 1·5. The sodium content, on the other hand, shows no change. The importance of this observation is enhanced by the further fact that while the sodium content of all carcinomatous tumours is about the same, the potassium content of primary cancerous growths is higher than that of secondary, and

the potassium content of squamous-celled tumours is higher than that of spheroidal-celled. Mottram has, therefore, shown that the cancer cell has a chemical co-efficient, but it is a modification in degree, and not in kind, of that of the healthy cell. These are the facts at present known about cancer cells as independent entities. We must now look at them as members of a community, and study their relations to neighbouring cells.

First we must notice *the disproportionate growth of the cancer cell.* It bears no relation to the growth, the needs, or the condition of the neighbouring cells and tissues, and, as it often tends to outgrow its stroma, and, by the pressure of its cells, to compress the capillaries, we have in this fact an explanation of the frequent degeneration, fatty and otherwise, of the cancer cells. The hæmorrhage which so frequently occurs in some cancerous growths may also be in part due to the same fact. The disproportionate growth of the cancer cell has been mistaken for evidence of its being an independent organism, but we shall see

abundant reason for rejecting this view and for being certain that a cancer cell is an altered body cell.

The pressure caused by the incessant and disproportionate *multiplication of the*

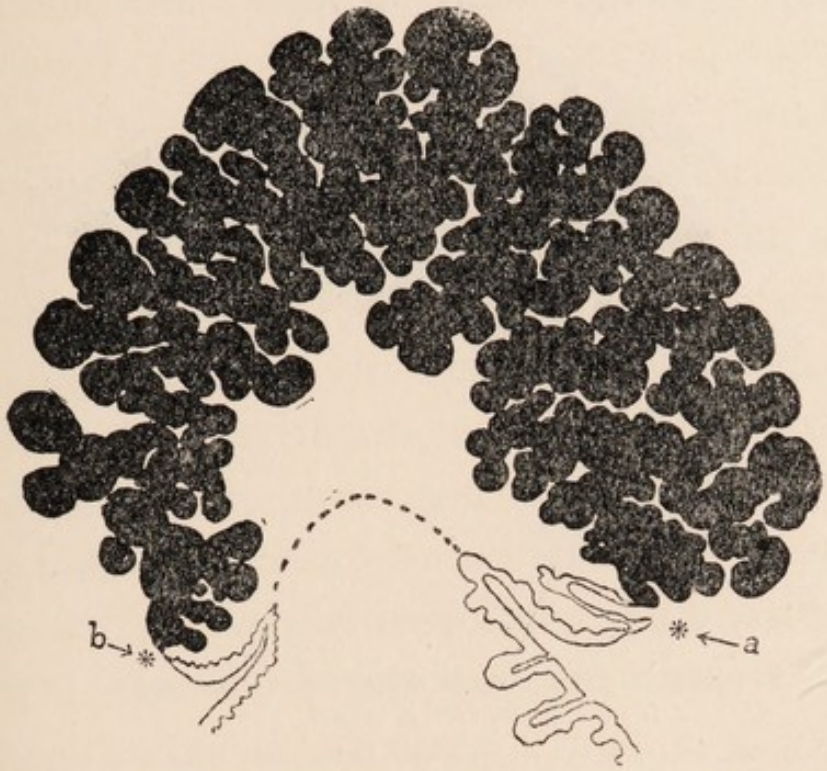


FIG. 1.—SQUAMOUS-CELLED CARCINOMA OF THE LOWER LIP IN A MAN.

The growth is a folded and crumpled sheet intercalated between the outer and inner surfaces of the lip. It shows folding of skin (*a*) and mucous membrane (*b*) over the margins of the growth, with great lateral displacement of the normal tissues adjoining either margin.

cancer cells causes not only complicated infoldings of the cancer itself, but flattening and distension of the adjacent soft tissues. In his second Scientific Report, Dr. Bashford has published drawings of

an epithelioma of the lip to show the enormous folding up of the cancerous parenchyma, and that what at first sight appears to be a solid infiltrating growth is really an immensely extended superficial growth, folded up into a ball, filling

FIG. 2.—SQUAMOUS-CELLED CARCINOMA OF THE LOWER LIP IN A MAN.

It shows sharp demarcation of the growth from the adjacent skin (*a*) and mucous membrane (*b*). At (*a*) the elongated epithelial papillæ of the skin are displaced by pressure of the growth; they are also being undermined and will be pushed off. At (*c*) the hair follicles already show displacement from pressure.

at first the narrow space it acquired for itself by pressing aside the yielding tissues of the lip, and then projecting on the surface (fig. 1). Bormann has shown that the papillæ immediately next the growing edge of an epithelioma of skin or

tongue are not exaggerated in size or cell activity, but are compressed and stunted (fig. 2). These observations run right athwart the commonly received notion that as soon as epithelial or other cells have acquired "malignant" properties they burrow deep into the surrounding tissues, and that the similar adjacent cells also show active growth and a readiness to participate in the disorder, as if "infected" by the malignant tendency. Unless Bashford's and Ribbert's statements are erroneous, they afford a demonstration that cancer cells in their growth give a qualified obedience to the law which regulates and controls the growth of the normal cells from which they are derived.

But if the first effect of cancer cells upon their neighbours is to compress them, their second and far more important power is to *invade the adjacent tissues.* This power of infiltration, as it is called, or permeation, is so well recognized that I need only mention it. The growth may penetrate even to bone and marrow, and, in doing so, cells, or groups of living cells,

pass into lymphatic or vascular channels, and are carried along by the slowly or swiftly moving stream therein, and may lodge in distant parts and develop into metastases. But they may not do so. Handley's studies of the process of lymphatic permeation have shown us that the passage of a cancer cell along a lymphatic is attended with great peril to it, the lymphatic endothelium has great power of cancer destruction, and for every cancer embolus that resists it successfully and thrives and multiplies—bursts through the lymphatic wall and develops as a metastasis—many a one falls a prey and dies. The same holds true of the hæmo-vascular embolisms. These have been studied by Borrel, Haaland, Bashford, Murray, Tyzzer, and others, and the resisting or destructive influence of the vascular endothelium on the cancer cells has been clearly demonstrated. The cancer cell when it wanders from its proper plane or sphere has to fight for its life; normally and in favourable conditions the "odds" are against it, and our *post-mortem* records bear abundant testimony to the ability of

the forces of resistance to these cell intrusions to limit the disease in many cases to the area originally attacked, even up to the death of the patient from the disease. While, therefore, we must not for a moment under-estimate the grave importance of the permeation of cancer and its tendency to develop metastases by the transference of the living cancer cells to distant parts of the organism, we must be careful to regard this in its due proportion, and to remember that all infiltration and every metastasis is only accomplished at a period later than the earliest onset of the disease and after the overthrow of very real natural resistance.

In this connection I would mention that cancer-bearing mice are not a favourable soil for the grafting of other cancerous tumours until the period at which they spontaneously develop metastases. In the earlier stages the resisting forces of the organism can hold at bay the cancer cells, whether spontaneously or artificially introduced into the tissues; in later stages either form of inoculation becomes potent. The occurrence of metastases is the

resultant of two forces—the vigour of the invading cancer cells and the resistance of the tissues to its development within them. This resistance may be inherited or racial, naturally acquired by age, artificially acquired—as shown by Bashford's experiments with the inoculation of various tissue-extracts—and it may be lessened by the persistent presence of a primary cancerous growth.

The influence of the cancer cell upon its neighbouring cells is strikingly shown by its *compelling them to form a supporting and vascular stroma for it*, of a type governed by the cancer cell and not by the stroma-yielding mesoblastic cells. Along with this, however, there is clear evidence that the surrounding cells exert an influence upon the cancer cell ; this is shown by its greater vitality and power of multiplication in the young than in the old, by its more active growth in certain races or families of animals, and by inoculability being limited to animals of the same species. Two other facts are also full of significance. In the experiments in the propagation of mouse cancer it has been shown

that when a graft is implanted in a fresh family or race of mice it grows with great difficulty, and that with each generation of grafts the success increases until it often reaches 100 per cent. This must not be confused with the increased virulence of an infective organism that may be produced by passing it through a series of animals, for the virulence of the cancer cell is only raised for the one particular variety of mouse and not for others. It is a subtle influence of the host upon the introduced cancer cell which makes it more congenial to the tissues of that particular variety of mouse. And then we have the remarkable fact that Bashford observed that in certain cases the repeated inoculation of an epithelial cancer stimulates the mesoblastic tissues of the host so intensely that the stroma becomes proportionately more and more abundant, and more and more richly cellular, while the epithelial growth lessens, until the carcinoma is replaced by a sarcoma. No more surprising, wonderful fact has yet been forthcoming from cancer laboratories than the demonstration of

this "transformation" of an epiblastic malignant growth into a mesoblastic cancer, the carcinoma exciting the development of a sarcoma, and thereby being itself destroyed. (See Plate III.)

What is the meaning of all this? Remember that the escape of epithelial cells into the tissues beneath them is a physiological process. Years ago Dr. Creighton demonstrated it in the case of the breast; he also showed that these permeating epithelial cells were destroyed in the lymphatics. Permeation is not a new power of cancer cells, although it exists in them in an unusual degree. I think we can recognize in the facts I have just mentioned evidence that *the cancer cell is not an alien cell; it influences, and is itself influenced by, its neighbours as a normal cell is.* The mutual adaptation and mutual influence of the cancer cell and its stroma surely speak of common descent—of blood relationship, if I may use that term.

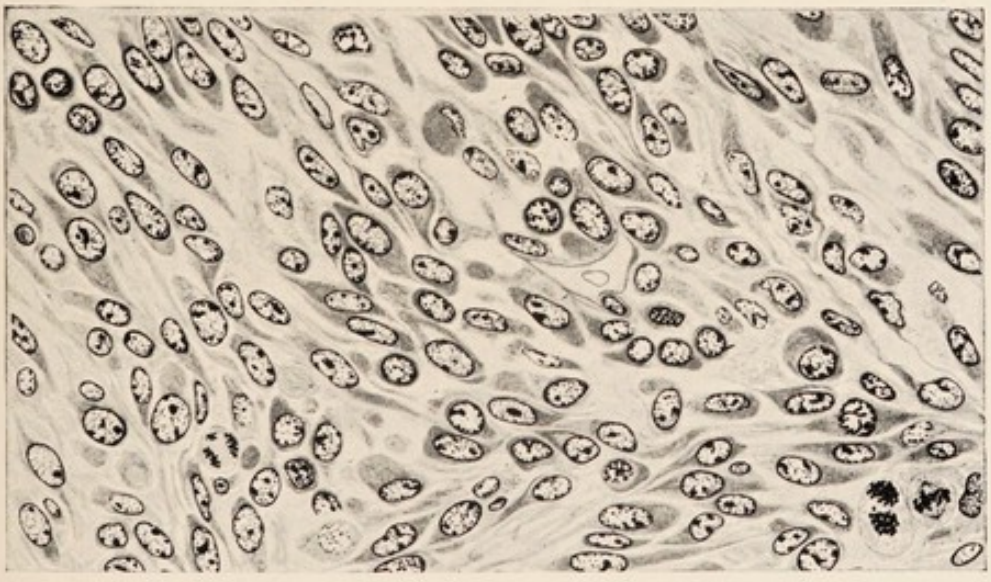
What is Cancer?

If, now, we attempt to piece together these various facts, what disease picture

PLATE III.—Showing transformation of carcinoma into sarcoma.

Carcinoma, showing alveolar character of parenchyma and delicate stroma.

Tumour showing great increase of a richly cellular (sarcomatous) stroma.



Tumour showing almost pure spindle-cell sarcoma.

To face page 40.

do they make? When we consider the intimate connection shown between cancer cells and the cells of the individual, and, perhaps, above all, the artificial conversion of a carcinoma into a sarcoma, we cannot recognize in cancer an independent parasitic growth, protozoal or other. Not only are the necessary evidences of the presence of specific pathogenic microbes absent, but both in broad outline and in particular detail the life-history of cancer is fundamentally different from that of the great host of known bacterial and other invasions. Nor is it possible any longer to see in cancer a reversion to the embryonic type of growth; that, before all else, is orderly, regular, with a long vista of development, differentiation, and functional activity. Cancer is cell life that is disorderly, irregular, with a minimum of development, differentiation, and function. Still less can we find a satisfactory explanation of this great disease in a circumstance so accidental, so trivial, as the sudden awakening into activity of entirely supposititious "embryonic rests."

What, then, is cancer? Before answer-

ing the question, think of the fertilized human ovum, a single nucleated cell. Picture it dividing into 2, 4, 8, 16, and 32 cells, all alike in size, form, and structure. Trace on these cells as they multiply by division and see them silently range themselves in the three primary embryonic layers—epiblast, mesoblast, and hypoblast —and by that step effect a separation of cells which to our senses appear identical, but whose destiny marks them out as absolutely distinct. Follow on the wonderful drama of development, try to realize the orderliness of it all, the varying differentiation of epithelia, endothelia, and connective tissues. Observe the intimate association of these embryonic layers in the evolution of parts and organs, their perfect co-operation, their mutual dependence. See the rising up here of mesoblast into papillæ, ever clothed with epiblast, and there the down-growth of epiblast or hypoblast into glands ever supported and nourished by mesoblast. Know that all this goes on with unerring precision, but with almost endless variation in proportion, with countless differences in form and

function of cell, with an ordered cycle of chemical changes so wide in its range, so varied in its detail, that we seem to be only at the threshold of a knowledge of it. Remember that this development proceeds with measured step to a certain definite extent only, that then in spite of all kinds of variation in supply and demand, and of adverse and favourable conditions, a certain level of cell life and growth is maintained for a more or less determined period, and that then first here, then there, the processes abate and fail, the flame of life seems to flicker until the unknown and wonderful changes of age draw on. I have failed to bring up before you a tithe of the marvels of the full development of a man from a single fertilized cell, or of the equally marvellous maintenance of his full manhood through the years of maturity and of the gradual decline into old age. But even in my faulty picture of it we see the outworking of a wondrous law, obedience to which brings orderly development, life, and health.

Now summarize our facts about cancer. Consider the disproportionate multiplica-

tion of certain cells, their imperfect, irregular, and useless differentiation, their failure to form Altmann's granules, their excessive affinity for and need for potassium, their insistent intrusion into surrrounding tissues, their imperfect co-operation with the other cells, and finally, their selfish greed which enables them to live when other cells are failing and perishing for lack of nourishment—what is it all but a failure of, or a revolt against, that great cytological law or impulse which first manifests itself in the primary division of the ovum, and lasts on till the death of the organism? Cancer is not a disease attacking the body from without, it is the result of a breach or failure of fundamental cell law; a law of which we know only the results; a law so majestic that obedience to it results in perfect development, perfect health, the full measure of days, and disobedience to it may slowly spell out all the inscrutable woes of cancer.

Causes of Cancer.

AGE.

Let us look now at certain conditions which are known to exert an influence on

the causation of cancer, and see what confirmation they afford to this view of the nature of cancer.

And first it is fully established that cancer is greatly influenced by age. In man its incidence rises with each decade after the third. Of animals this is as true

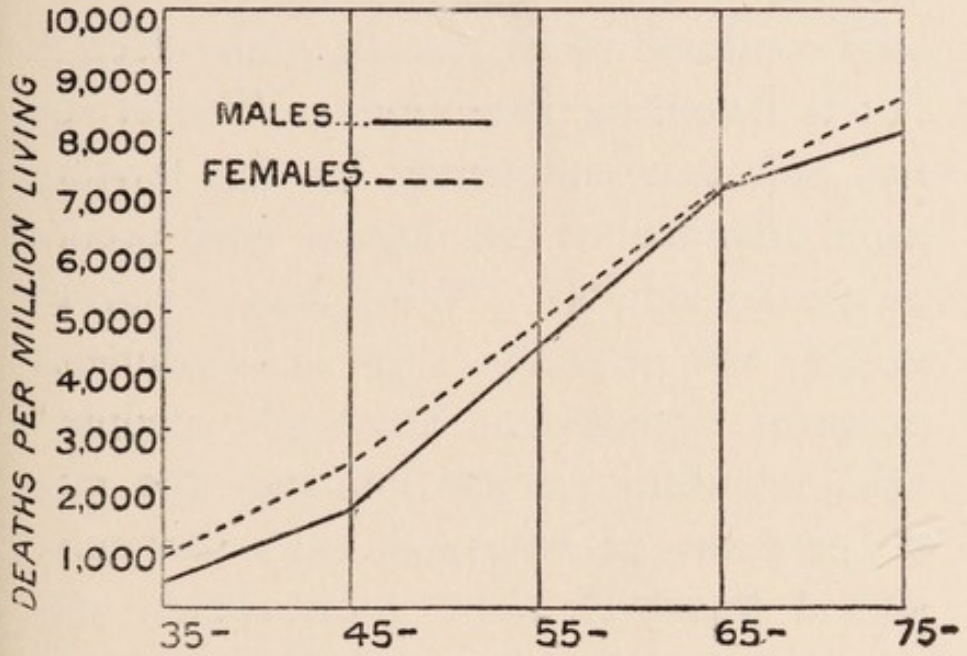


FIG. 3.—Mortality from cancer per million living at each of five groups of ages from 35 years upwards (1906).

as of man. Thus the average life of mice in laboratories is three years, and sporadic cancer occurs almost invariably only after they have reached the age of two. It is from India, where the cow is a sacred animal, and is allowed to live to old age, that we have most evidence of the

occurrence of cancer in that animal. What we have so long known in the case of man, therefore, is not in any sense an "accident" or peculiarity in him—it is one of the fundamental facts of cancer. Cancer is undoubtedly a disease that generally arises in cells that are growing, or have grown, old. But senility of tissue is not a necessary condition of its growth, and indeed is not a favouring condition. Who of us has not been impressed by the terribly rapid advance of the disease as it occurs in young adults? Who has failed to notice the equally slow and difficult progress it makes in some old people? Of all conditions which influence the rate of progress of cancer in any particular site, I know of none more potent for mischief than the youth of the individual. From the cancer laboratories we get definite statements that it is in young mice that cancer grafts grow with most certainty and with most rapidity. So important is this that Bashford has had to point out that, before a just comparison can be made between the results of inoculations under varying circumstances, it is

absolutely essential that the experiments should be carried out in animals of known age and of the same age. Now this fact —supported alike by clinical human experience and by experimental animal experience—teaches us that the condition precedent to cancer is not in the nutrition of the tissues outside the cancer cell but within the cancer cell itself. The external conditions for the growth of the cancer cell are more favourable in the young than in the old, and a cancer cell having once started on its errant course can profit to the full from the greater nutritive vigour of the young. Incidentally this fact is a strong indication that cancer is not an infective disease, allied to bacterial invasions. So far as is known of them, old age is not a favouring factor; and it is the veriest negation of all our knowledge of these diseases that a condition favourable to their origin is unfavourable to their spread.

SEX.

It is well known that cancer is more frequent in women than in men, and that

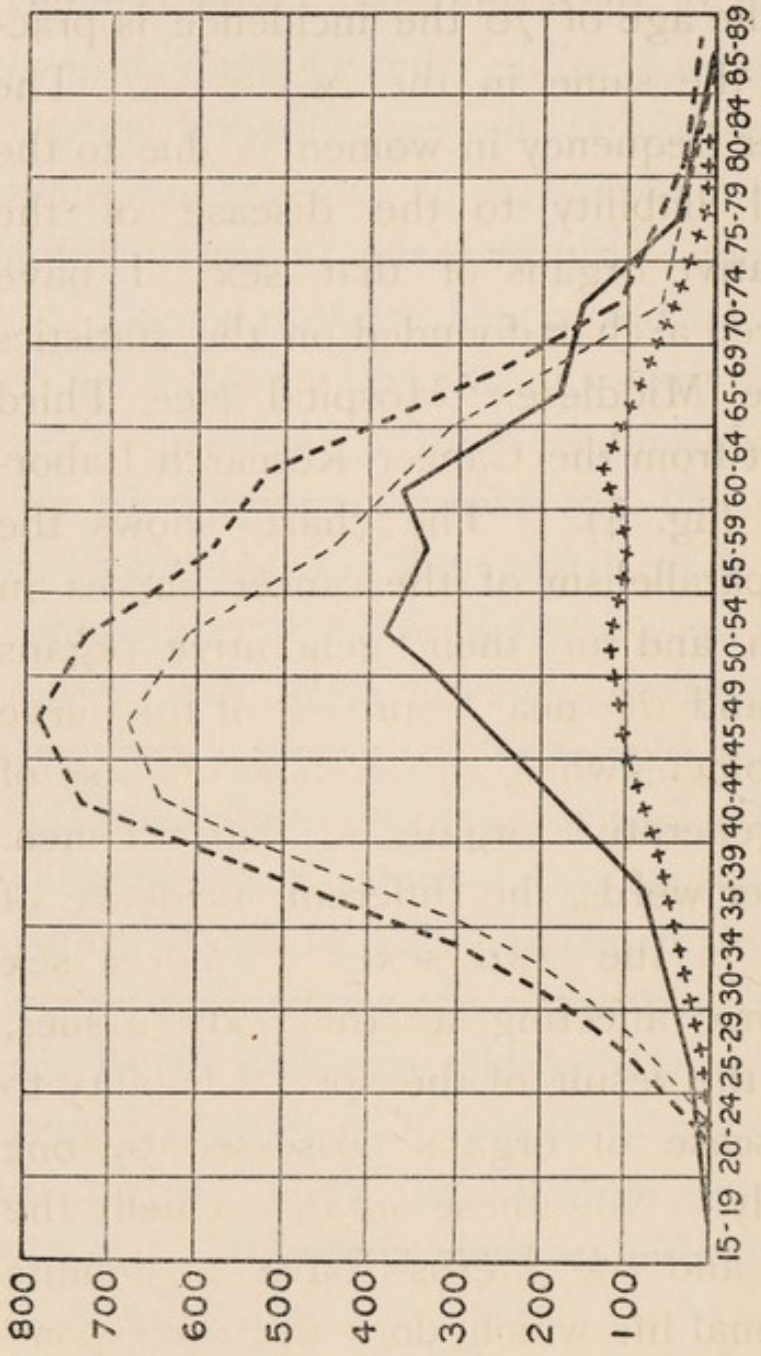


FIG. 4.—Unbroken line ——— cancer in males. Thick broken line — — — cancer in females. Thin broken line — — — cancer of uterus, vagina, vulva, and breast only. Crossed line × × × cancer in females, excluding cancer of uterus, vagina, vulva, and breast.

its incidence increases earlier, and attains its maximum sooner in them than in men; after the age of 70 the incidence is practically the same in the two sexes. The greater frequency in women is due to the special liability to the disease of the generative organs of that sex. I have prepared a chart founded on the statistics of the Middlesex Hospital (see Third Report from the Cancer Research Laboratory) (fig. 4). The chart shows the close parallelism of the cancer curves in women and in their generative organs only, and the near approach of the curve for women, when we exclude disease of their generative organs, to that for men. In other words, the different incidence of cancer in the two sexes is not a sex difference affecting all the body tissues, but is the result of the special liability to the disease of organs possessed by one sex only. Now these organs—chiefly the breast and the uterus—have a definite functional life which does not correspond at all with the life of the individual, but starting at about 14 usually begins to terminate about 50, and during those

years these organs are the seat of frequently repeated periods of great cellular activity followed by periods of decline and atrophy. It is, I believe, because of this fact, that these organs are specially prone to cancer as they get old —before the rest of the women ages— and in this we see the explanation of the facts that cancer is more frequent in women than in men, and that its age-incidence differs in the two sexes.

CHRONIC IRRITATION.

Of the reality and importance of chronic irritation as a condition precedent of cancer I cannot stay to speak, nor need I, the facts are too well known. Attempts have been made to find the underlying cause of cancer when it follows chronic irritation in some change in the sub-epithelial tissues, and the Hunterian lectures of my colleague, Dr. Victor Bonney, on this subject are no doubt fresh in your memory. He showed that interference with the continuity and perfection of the subepithelial elastic tissue layer always precedes a carcinomatous

growth, and, conversely, that cancer never originates in perfect normal tissue. It has been objected that his beautiful preparations fell short of a demonstration that the changes shown were antecedent to the earliest development of cancer, and and that they were as compatible with consequence as with precedence. It is, however, surely a striking fact that these changes are only met with at the seat of the primary growth and in the nearest lymphatic glands, and not in the true secondary growths. But while accepting Dr. Bonney's demonstration, I think we cannot for a moment regard any change in the subepithelial tissue of a part as the sole or most significant change in what have been well called "precancerous conditions." The essential features of such chronically irritated and precancerous tissues are increased cell formation associated with defective differentiation or cell development, and the changes in the subepithelial tissues may be either a result of this or another expression of similar nutritive changes.

The cytological effects of what we call

chronic irritation are essentially two—increased cell multiplication and defective intracellular metabolism. Now the life of a cell is not to be expressed in periods of time, but in terms of its multiplication or proliferation. An epithelium does not become old because its individual cells have existed for a particular length of time, but when the multiplication of the cells necessary for its maintenance has been repeated a certain great number of times. Therefore chronic irritation, by adding to the frequency of cell division, produces the special condition of cellular old age; it is, indeed, equivalent to the ageing of a tissue. Its other effect is equally significant. The imperfect cell development and metabolism carried on for generation after generation of cells is clearly akin to senile defects in cell growth and metabolism, as shown, for instance, in diminished secretion and in the impairment of all nervous functions. The word "irritation" is rather apt to suggest a stimulating process; it is important to remember that chronic irritation is the most effective mode of hastening on

changes closely akin to, though not identical with, those of old age—the conditions in which we have seen cancer to occur most often.

X-RAYS.

Prolonged exposure to X-rays may undoubtedly cause cancer. The evidence of the influence of X-rays upon cell life is most important. Lazarus-Barlow and Somerville Hastings have shown that in the ova of Ascarides exposed to X-rays the division of the cells is more rapid than in "controls," while fewer of the ova come to maturity. If we look at the hands of an X-ray worker we see the same thing—increased production of epidermic cells, with imperfect development of the too numerous cells. Think of this process carried on and on; will it not cause a premature ageing of the formative epithelial cells, associated with an imperfect elaboration of the cells?

ALCOHOL.

The last etiological factor to which I can refer is alcohol. To some extent this causes cancer by directly or indirectly

inducing chronic irritation ; but let us note that alcohol is a protoplasmic poison—that is, a substance which directly interferes with, and mars, cell metabolism and cell life. The influence of alcohol on the incidence of cancer is really important. Dr. Tatham's statistics of the mortality of various occupations from certain diseases revealed the fact that cancer is twice as frequent among brewers and London publicans as among clergymen, and that the cancer incidence in any trade varies with the attendant habits as regards alcohol. Dr. Newsholme has dealt with this subject in the light of figures obtained from the United Kingdom Temperance and General Provident Institution, and has shown that the mortality from cancer among the insured in that institution, if represented by the figure 100 among the non-abstaining males, would be represented by 72 among the abstainers. He laid emphasis upon the fact that this statement was based upon scanty evidence ; I have, therefore endeavoured to increase the evidence, and Sir Thomas Whittaker has very kindly brought the

United Kingdom Temperance and General Provident Institution.

Ages of insured persons and of persons dying in each group	Aggregate population or years of life at risk during years 1891, 1896, 1901, and 1906		Deaths during the Years 1891, 1896, 1901, 1906						Ages
			From all causes		From malignant disease		From malignant diseases (males alone)		
	Abstainers' section	Non-abstainers' section	Abstainers' section	Non-abstainers' section	Abstainers' section	Non-abstainers' section	Abstainers' section	Non-abstainers' section	
Under 24 ...	2,314	445	6	2	—	—	—	—	—24
25—34 ...	8,559	4,140	23	23	—	—	—	—	25—34
35—44 ...	13,406	9,005	58	58	1	4	1	4	35—44
45—54 ...	15,645	13,571	143	177	20	14	20	14	45—54
55—64 ...	12,475	14,000	229	365	20	38	20	33	55—64
65—74 ...	6,858	8,833	301	516	22	64	20	50	65—74
75 ...	2,121	2,736	274	408	13	20	12	17	75
	61,378	52,730	1,034	1,549	76	140	73	118	

figures up to date; and the accompanying table, which is prepared in the same manner as that given by Dr. Newsholme, shows that from the larger number of lives the same conclusion is to be drawn.

It comes to this, then, that all these so-called causes of cancer—age, chronic irritation, X-rays, and alcohol—agree in being conditions that wear out the cells of a part; they add to the number of cell generations, they deteriorate the evolution of the individual cell, they appear to lessen the hold over the cell of the great primal cell law, and so they cause cancer.

Primary Cancer not always Single.

One objection that may well be raised to this view lies in the occurrence of primary cancer as a single lesion. It is easy at the first blush to find in this a complete refutation of what I have been trying to establish. But the more I have thought of this objection the less convinced I am of its worth. A physiological essay *de senectute* would be very valuable. Wherein lies the true essence of senility? Is it simultaneous in all our tissues? Are

we animated illustrations of Oliver Wendell Holmes's "wonderful one-hoss shay"? And if not, if one organ or tissue may grow old before its fellows, are we quite wise in holding that all the individual cells of a given organ must grow old together?

But *cancer is not always single in its primary seat.* My colleague, Dr. Young, among others, has published in the Fourth Report of the Middlesex Hospital Cancer Research Laboratory a number of instances of multiple primary cancer. In my limited experience I have seen such cases as these: in one case a woman presented three cancerous growths in her left breast, all of them noticed about the same time, no one of them much larger or notably different from its fellows. Three times I have been consulted by women with a tumour in each breast, small, far distant from each other, and, except for enlarged glands in the axilla, without evidence of metastasis, so that I could only regard them as simultaneous primary cancers. One of these patients submitted to amputation of both

mammæ in 1899, and has remained without recurrence until now, so that it is reasonably certain that in her case one breast was not infected from the other. Many times I have seen cancer occur in the breast at an interval after removal of the opposite breast when there was no evidence of metastasis elsewhere, and the subsequent progress of the case was so exactly similar to the disease occurring in one breast only, that I was forced to see in it a new attack of the disease, and not the development of a metastasis from the earlier tumour. Twice over it has happened to me to be called to do colotomy for chronic intestinal obstruction that had become complete, and in which examination of the rectum revealed a stenosing growth within easy reach of the finger, but further examination showed a second independent, annular, carcinomatous growth, in one case in the descending colon, and in the other in the transverse colon.

Last year I was consulted by a patient whose left breast had been removed for cancer in 1902; she had had three subse-

quent operations. She came to me complaining of an extremely severe pain along the distribution of the ulnar nerve, and I found a very dense and firmly fixed mass of growth close to the coracoid process. I advised her to try what radium would do to relieve her pain ; immediately after exposure to radium for forty-eight hours, carried out by Dr. Finzi, she lost all pain in the arm and hand, and it never returned. The radium was applied on a few subsequent occasions in the hope that it would lead to the disappearance of the growth—of this happy result I saw no proof ; but meanwhile an epithelioma developed in the left labium majus, ran a rapid course, and was the cause of her death in December, 1909.

In the lip I have, on several occasions, seen two or more quite independent primary growths, and in June last I saw a very early epithelioma of the tongue which proved, when subsequently removed by Mr. Spencer, and examined by Dr. Bashford, to be starting from four separate centres. Of multiple rodent ulcers I have had very numerous instances. Multiple

epithelioma in lupus and in X-ray dermatitis is also well known, and from Kashmir we are told of multiple kangri cancer.

Were I, on the other hand, to try to give you any adequate conception of the irregular incidence of old age, I should need a separate lecture and a much wider knowledge than I can even pretend to possess. But let us take one example —and that the best known of all, the hair —what numerous varieties in the senile changes in the hair we see! It may fail to grow without change of colour; it may lose its colour and persist in growth, again, these variations may affect the hair only in one part of the body, or in small areas only, or even be limited to the product of a single hair follicle. If age can thus influence the growth of certain hair-forming epithelium, why may not the age-effect that leads to cancer start in a single epithelial cell?

Immunity.

The only other aspect of the cancer problem to which I would refer is ex-

pressed in the word *immunity*. This word is specially associated with the processes by which we are enabled to withstand successfully the attacks of pathogenic organisms. It is clear, however, that if cancer is not due to any similar cause, but arises from a failure to continue the cellular development of a part exactly in accordance with the pattern of normal growth, we must not look for immunity from this disease along the lines in which we find it for infections. Careful search by many observers has failed to find evidence in cases of cancer of the activity of those protective forces which play so great a part in the life-history of infective diseases. In the last Croonian lecture at the Royal College of Physicians, Dr. Andrewes gave a very full account of the part played by leucocytes in protecting against infection. There is no like tale to be told of their activity and power against cancer. Blood changes there are in the *late stages* of the disease, when other factors than the presence of a malignant growth are active, but none of a protective character have been

demonstrated in the early stages of cancer, when that disease alone is present to disturb the harmony of nutrition. We have in this another fact which strengthens the contention that cancer is not an infection disease. If the disease differs wholly in nature from those infections in which immunity has been chiefly studied, the problem of cancer immunity will also be different.

Accepting the view of cancer that I have tried to submit, cancer immunity might be evidenced in one or more of the following ways :—

(1) The power of living cells to conform to the law of normal development and to avoid that increased multiplication, defective differentiation, and tendency to intrude themselves into, and grow among neighbouring cell territories, which together connote cancer.

(2) Opposition to the intrusion of cancer cells into, and their development in, heterologous tissue.

(3) Inhibition of the growth of cancer and destruction of living cancer cells.

What can we say under each of these

heads? Do clinical experience and experimental pathology throw any ray of hope across the dark sea of malignant disease? They do. The deep impress of the primal law of development holds the cells of our tissues in true and loyal obedience to the very end, in the almost infinite majority of cases, and in the great majority of individuals. The incidence of disease, and immunity from its initial attack, are of course complementary, and the same fact can be expressed either in terms of disease or in terms of immunity. Thus the public have been distressed by the oft-repeated statement that 1 out of every 8 women who reach the age of 35 dies subsequently from cancer; and of the men who attain 35 years, 1 of 13 dies from cancer! This no doubt is true, but we can express the same fact in terms of immunity, and say that 7 out of the 8 women, and 12 out of the 13 men of 35 years of age, will not die from cancer! This is the great initial fact of cancer immunity—that in spite of added years, and of all the unfavourable conditions which tend to wear down the obedience

of cell life to its fundamental law, 90 per cent. of men and women who pass down the hill of life hold this dread enemy at bay.

Of the second kind of immunity—the opposition to the intrusion of cancer cells into the heterologous tissue—we have plenty of evidence. There is first of all the difficulty in cancer grafting, and then the fate of many of the cancer cells and minute cancer emboli that get into lymphatics and blood capillaries ; the majority of them are overwhelmed by the opposing influence of the endothelial cells, and only one here and there is ever able to survive. Or let us recall our clinical experience of the very slow progress of many cancers, of their long-enduring limitation to their primary site, in some cases, and of the extraordinarily long period—amounting to ten or even more years—that may elapse between the removal of an active cancer and the development of a metastasis. Do not all these well-established facts tell us that the organism is not left powerless, defenceless, before the intruding cancer cells, and that the opposing

foes are not so unevenly matched as students of the failures of these saving powers would persuade us? There is a force of immunity which can protect, and does protect, against the chief mischievous power of malignancy ; and when a surgeon asserts that every case of cancer can be cured by a sufficient and sufficiently early operation, I can assent when I remember the reality and efficiency of this force of immunity, which is his great ally.

The third form of immunity is what is popularly known as the "cure of cancer" —*the disappearance of cancerous growth.* Those who are studying the disease in mice report to us that in these animals it is quite a frequent occurrence for a grafted cancerous growth, after attaining some size, to slowly shrink and disappear, and in some series of experiments a large proportion of the grafts that have "taken" have, after a period of growth, spontaneously vanished. Among the 500 sporadic cases of mouse-cancer observed by Bashford, this event has been witnessed only two or three times. In human pathology, I fear, it is a still less frequent fact, *but*

it undoubtedly is observed. It is most frequently seen in the gradual absorption and disappearance of small secondary nodules in the skin and subcutaneous tissue. It is occasionally witnessed on a grander scale. Many years ago I showed a patient at meetings of the Clinical Society of London, who recovered spontaneously and completely when she seemed to be at death's door from cancerous deposits in the lung and the neck of the femur, secondary to cancer of the breast. She remained well for several years; unfortunately, I have been unable to trace her for the last four years. (*Clin. Soc. Trans.*, vols. xxx. and xxxii.) More recently I have had an equally satisfactory and striking case.

A woman, aged 52, was admitted to my cancer ward of the Middlesex Hospital on February 28, 1906, suffering from advanced cancer of the uterus; that organ was fixed in the pelvis, the cervix was ulcerated, and masses of growth were felt invading the anterior wall of the rectum; she suffered from constant discharge and irregular hæmorrhages. In February, 1907, I find this note: "The

vaginal cervix is the seat of a nodular growth, which is hard, but apparently not ulcerated; it extends all round the cervix and infiltrates the posterior wall of the vagina and anterior wall of the rectum. There is also some extension down the left vaginal fornix. The uterus is fixed." She became slowly but steadily worse, and for many months was unable to leave her bed, owing to frequent hæmorrhages and the consequent weakness, and the pain which movement increased. In the early summer of 1908 she gradually lost the use of her lower limbs, and the paralysis extended to both upper limbs until she was literally unable to move hand or foot, My colleague, Dr. Campbell Thomson, kindly examined her on several occasions and satisfied himself that the paralysis was due to exaggerated peripheral neuritis. During the late summer she improved, and when I returned from my holiday at the end of September, 1908, I found that she could just move her hands a little; she was also stronger, with less pain and less discharge, and a local examination showed that the

uterus was less firmly fixed than before. Not to weary you with details, the patient got quite well, all the local evidences of disease vanished, and I made this note in July, 1909: "Uterus is small, senile; vagina narrowed at its upper end, vaginal cervix very small, no ulceration or growth to be felt in cervix or vagina; uterus is mobile. The original disease has entirely disappeared."

After keeping her for several months to make sure of her recovery we had to discharge her from our Cancer Charity as she no longer filled the necessary condition of suffering from cancer, and she now earns her living by needlework.

No treatment specially directed to the cure of the disease was employed in this case.

Here is another case :—

"A trained nurse discovered a lump in her left breast in 1896, when she was aged 46. In June, 1897, Dr. Anderson, of Faversham, removed the breast, and in September, 1898, he removed a lump from the axilla. In January, 1899, she came under the care of Mr. Farnell, of

Eastbourne, who removed a recurrence in the axilla and two or three nodules in the skin. In May of the same year he thoroughly cleared out the axilla, as there was evidence of more extensive disease there. In November, 1898, and in March, 1900, he excised small recurrences in the axilla. In May, 1900, he again operated on the axilla and found it impossible to remove the growth under the arm. I saw this patient in September, 1900; the wound in the axilla was unhealed, and there was a firmly fixed mass of growth just below the clavicle; the upper limb was greatly enlarged from œdema. Mr. Farnell and I advised the patient to submit to double oöphorectomy, which was forthwith carried out. The wound quickly healed; the œdema of the arm and all evidence of the presence of a growth disappeared. I saw this patient last month, after an interval of ten years, and found her enjoying excellent health; the scars of her numerous operations are the only sign that she has ever been the subject of cancer.

Here is another case:—

"A single woman, aged 41, was admitted, under my care, in January, 1900, with cancer in both breasts. The disease had been noticed on the right side for two and a half years, and there had been ulceration for a year and ten months; on the left side it had been known to exist for six weeks, and the lump had doubled in size in that time. The disease infiltrated the entire right mamma and the skin covering it, and fixed the part to the ribs beneath; there were enlarged glands in the right axilla, and beneath the lower end of the right sterno-mastoid muscle. Several nodules of secondary growth were scattered around the primary growth, and above the nipple was an ulcerated surface measuring 2¼ in. by 3½ in. There were also two areas of marked venous congestion of the skin, one below this breast and one over the pectoral muscle towards the point of the shoulder. In the outer part of the left mamma was a firm infiltrating mass the size of a large walnut, and in the left axilla were enlarged and tender glands. On January 31 double oöphorectomy was carried out.

Within three weeks the congested areas I have mentioned had become pale, the ulcer was healing, and the secondary nodules were smaller. By March 9 there was no nodule to be felt in the left breast, and I could only detect in that axilla one tiny gland the size of a buck-shot; on the right side the lower half of the breast was free from all evidence of growth, and the ulcer was healed. By March 27 all that was left of the originally extensive disease were two or three very small nodules in the skin of the chest. On April 18 symptoms of intestinal obstruction developed, an operation was performed, and I regret to say that the patient died quite suddenly while some adhesions were being separated. At the necropsy a few small nodules of growth were found in the subcutaneous tissue over the right breast. No other traces of cancer could be detected. A nodule removed in March presented characteristic appearances of spheroidal carcinoma with a relatively large amount of connective tissue.

Here is another good case :—

A woman, aged 57, was first seen by me in July, 1903. Her left breast had been removed for carcinoma in April, 1900; four operations for recurrence had been performed since. There was a very considerable local recurrence, enlargement of the third costal cartilage, and deposit in the lower flap and under the arm. She was treated with X-rays combined with the internal administration of oxide of silver. All the growths have disappeared, the patient is in good general health, and continues at her work. I have seen her from time to time during the last seven years, the last time in October of this year; she was then quite well, except for a little superficial ulceration, which was possibly due to the treatment that had been employed.

Here is a somewhat similar case:—

A woman, aged 44, was first seen by me at Middlesex Hospital in September, 1909. Her right breast had been removed for carcinoma. There was an extensive secondary deposit in the chest wall with a wide and deep ulcer. Under X-ray treatment this ulceration

rapidly cleaned and healed, and the growth has disappeared, leaving a very little thickening to be felt where before there was a mass of deposit. Her health is quite good and she does her usual work.

A woman, aged 43, was first seen by me in May, 1909. Her left breast had been removed for carcinoma. There was a considerable secondary mass of growth in the lower flap and under the axilla. Under X-ray treatment the deposit has steadily decreased in size, and in November of this year there was only a slight thickening to be felt. Her health is good and she is doing full work.

A man, aged 44, was sent to me from another hospital as an incurable case in December, 1903. A columnar carcinoma of the rectum had been removed by Kraske's method. There was local recurrence of the disease, and a mass of growth the size of an orange projected from the sacrum. He was treated with X-rays. Thirteen months later—January, 1905 — the following note was made: "Good general health, doing all his work (as a postman), no sign of disease." In

August this year (1910) he was seen again, and gave this history. At the end of 1905 there was noticed a warty condition of the old scar; this ulcerated. It was removed, and proved to be a squamous epithelioma. The wound healed well, and he has had no further trouble.

He continues his work as a postman, and enjoys good health. He was seen in October of this year, nearly seven years after his first visit.

Several years ago I excised the left superior maxilla of a woman for cancer. Some months later her attendant in the country sent her back to me at the hospital with extensive recurrence; the cavity left by the removal of the bone was filled with a mass of growth. A year later the doctor asked me to see his patient again, and to my delight I found her in excellent health, and without a trace of the local disease. No "special" treatment had been employed.

Another case that I can never forget was that of a woman who had had her left breast removed for cancer and subsequently came to the Middlesex Cancer

Charity with local recurrence, growth in the glands of the neck, and a large brawny arm. She got quite well, and was able to earn her living again at the wash-tub. I had another similar case where the "brawny arm" got quite well, and all the recurrence of the disease disappeared. These cases were treated with X-rays. I have recorded the details of a case of melanotic sarcoma in which very numerous secondary nodules disappeared, enlarged glands shrank, and impaired health notably improved so that an invalid became able for some months to resume his work on the Stock Exchange (*Middlesex Hospital Archives*, vol. ix.).

The Hope of Cure.

This is not an exhaustive list of such cases that I have myself seen, and I am sure that my experience is not singular. In some of them the disease was not "cured" in the sense of being wholly and permanently removed, but in several there is strong reason for thinking that this word "cure" may be justly used. In many of the cases treatment directed to

this end has been carried out; in some there has been no special treatment. In my brief records of these cases I have not discussed the treatments employed, because my present purpose is not to vaunt a remedy but to state a fact—that cancer, even when advanced in degree and of long duration, may get better, and does sometimes get well. *There is cure of cancer apart from operative removal.*

All therapeutic cures are obtainable only by the working of physiological forces, and the first hope of therapeutic success comes with the observation of the efficiency of unaided Nature to accomplish cure. You may say to me there is little comfort in all this; you enunciate a philosophical concept, and you tantalize by a record of very rare exceptions in the grey, grim drama of cancer. Not so. These cases, rare though they be, are the sun of our hope. In the darkness of night it is everything to know that there is a sun towards which the earth is revolving, and that if we fix our eyes on the East we shall certainly see the grey promise of dawn and then the many-coloured heralds

of the golden sun itself. And as the victims of cancer call to us in the dark night of despair, "Watchmen, what of the night," oh! it is much to know that for cancer-stricken man there is also a sun of healing. We are apt to envy the astronomers who know so well the laws regulating the movements of the spheres, that they foretell the happenings of the universe with a precision that is the despair of workers in other branches of natural science. But with all their knowledge of these laws they cannot hasten on the day, or affect in one small circumstance the movement of a planet, or alter the destiny of a single grain of meteoric dust. But when the biologist shall know the laws that govern cell growth, with a knowledge akin in its sweep and accuracy to that of the astronomer, he will have power, and that power will enable him to prevent, to control, and to cure, cancer.

JOHN BALE, SONS & DANIELSSON, Ltd., 83-91, Gt. Titchfield St., W.