The present aspect of the cancer problem / by Roswell Park.

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Professor of Surgery Medical Department, University of Buffalo

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The most important problem in thology of to-day is still the cancer oblem. It is likewise the most crutable. It continues to engage, as must, the attention of all students pathology and research workers, d never was it attacked from so ny different directions as at pre- t. Although, so far as final solu- n is concerned, it still remains the dle of the ages, nevertheless a great al of light has been thrown upon perplexities by research of the past v years. In this systematic in- stigation New York State has been e pioneer, and the Cancer Labora- y, now working as a department the New York State Department Health is, as it has been since its ganization five years ago, an ex- edingly active center for such in- stigation. The studies which have oceeded from this laboratory have gaged the attention of the most rnest thinkers the world over, and ve given prominence to the effort ere making to solve at least some of e moot questions concerning this ead disease.

Five years ago, when endeavoring secure state aid for this purpose, I lled attention in a variety of ways d in different publications to the ady increase in the disease, taking for the purpose at that time the population of New York State, and showing what a rapid increase in mortality could be noted, decade by decade, in the State Board of Health returns. Incidentally the position was taken that this increase concerned not New York State alone, but a large part, at least, of the civilized world. These statements had a force which was almost dramatic and were challenged in various places and by various writers. They stand to-day practically unchanged after all the assaults made upon them, and more than this, confirmed by statisticians at home and abroad, who have not been able to explain away the figures presented by any theory save that including the actual fact. Maps and figures have been published in Great Britain, in Germany, and in many States of this country, which fully corroborate the general statements that I made some years ago. The force of the argument is not lost, even supposing that the critics are in some measure correct in the statement that the increase is to be explained largely on the ground of improved diagnosis. For if this be so, while the rate may not be increasing quite so rapidly, nevertheless it shows what a number of deaths are actually occurring from

this disease, and stamps it as equally important and equally deserving the attention of the highest sanitary and public authorities. In this connection, and without wearying you with figures, I would simply like to call your attention to some figures gathered by a perfectly unprejudiced student of the subject, Dr. F. F. Simpson, of Pittsburgh, Pa. Early in 1901 he addressed notes to the Boards of Health of many of the larger States of this country requesting facts regarding population, the total number of deaths, and the number attributed to cancer for each year from 1890 to 1899. From these official reports it would appear that for 1899, twenty-two States with an aggregate population of 9,359,600 reported their total deaths to be 169,608, while their deaths ascribed to cancer aggregated 5,486. It therefore would appear that of all deaths in those States for that year, one in every thirty-one was due to cancer. If we accept the view that almost all deaths from cancer occur in those over thirty, and accept at the same time the data upon which life insurance companies base their risks, viz.: That 56 per cent. of deaths occur under the age of thirty, we are safe in the conclusion that of all who die over the age of thirty, one in fourteen dies of cancer.

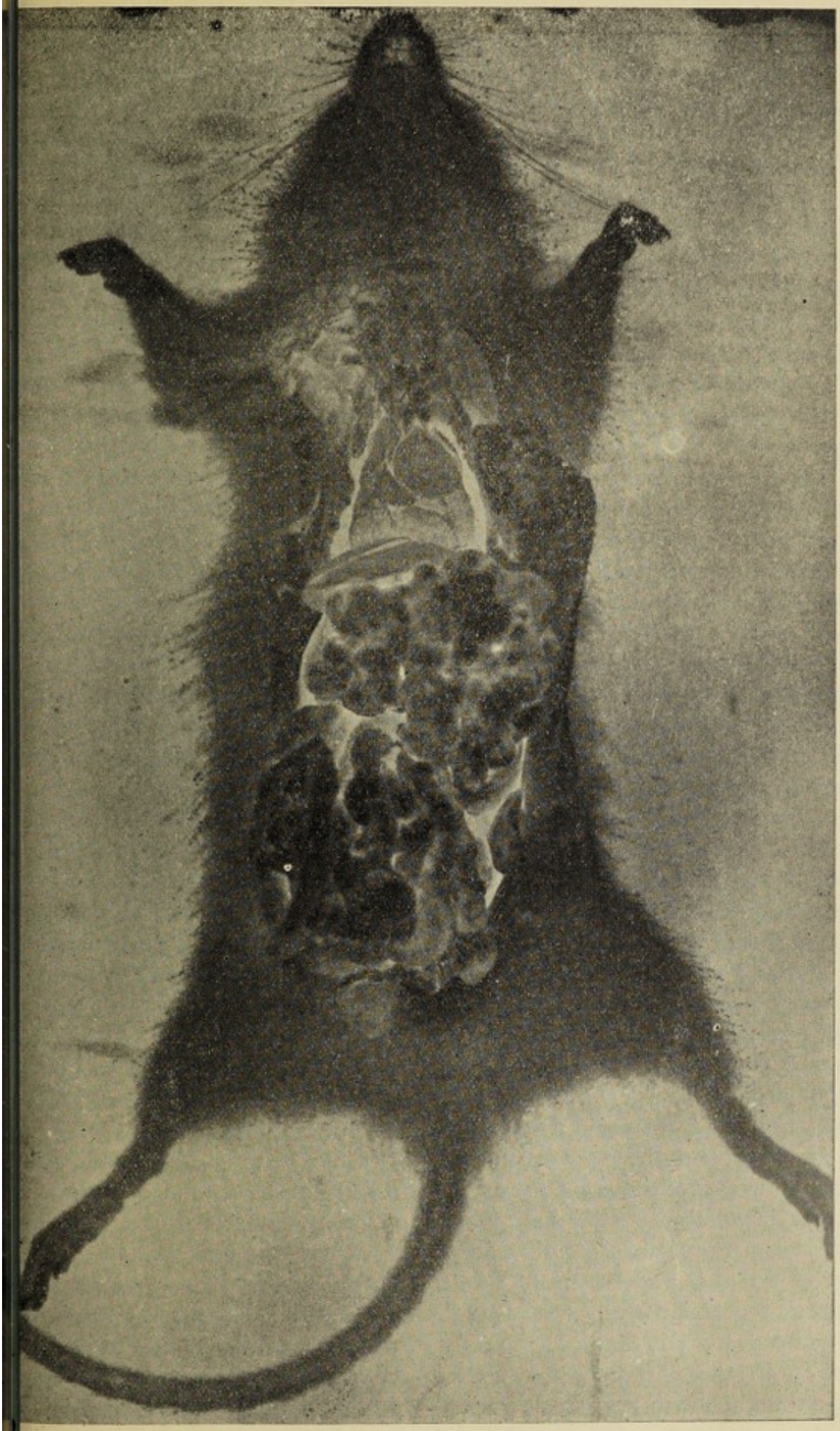
Out of a number of tables which he prepared, there is one showing the relative number of deaths from cancer and from all causes in the years given, most of this information coming from the U. S. Census reports.

1850—1	death from cancer to		156	deaths from all causes	
1860—1	"	"	109	"	"
1870—1	"	"	79	"	"
1890—1	"	"	47	"	"
1900—1	"	"	35	"	"

From this it will appear that wi
the past fifty years the proportio
deaths from cancer has risen
one in 156 to one in thirty-five,
round numbers is five times gr
than in 1850. These figures
startling, and, moreover, have
corroboration of independent o
vers in several different parts of
world.

But statistics make poor readi
public, and I am quite willing t
the current literature of the day
stantiate all that I have claime
this direction.

With regard now to the natu
the disease, the problem ma
summed up, I think, in these w
Cancer is cell anarchy or cell re
tion, if you will, provoked by
agency. When we know the
nature of this excitant, we shall
the basis for our work. It must
however, either from within the
or from without. What it is
makes cells act in the way in which
do in this disease, is the great
tion. The evolutionists and the
tologists have been trying to
this problem, either on broad ge
considerations, or by examini
through the microscope, and both
missed the very important clinica
which we cannot afford to miss
are to square ourselves wit
Absolutely no explanation is aff
for this peculiar cell activity
can come from within the cell
Neither atavistic tendencies, he
ary influences nor any other exp
tion which can be framed in
suffices for this purpose. The
and can be but one explan
some extrinsic influence broug
bear upon the cells alone suffic



RIMENTAL TRANSMISSION OF SARCOMA (INTRAPERITONEAL) FROM RAT TO RAT. L. LOEB.

explain their morbid activity. Summed up in its comprehensive significance this means the parasitic theory of cancer, which has not yet been reduced to a question of what parasite, but rests at present upon the broad and indefinite plane of mere parasitism. Histologists and the old line pathologists who adhere to conventional views will never decide this matter. It must be viewed from a wider standpoint than that afforded by the brass tube and the lens at either end of it. I cannot help repeating here the fact to which I have more than once publicly alluded, that there is no other disease characterized by metastasis in which the pathologist declines to see a parasitic, *i. e.*, an infecting and infectious agent. Why is it then that he refuses so blindly to see it in this particular instance? There is no other disease even characterized by progressive infiltration which has not a parasitic cause or a parasitie as a cause. I should keep repeating my own agruments were I to rehearse here all that might be said in favor of the parasittic hypothesis, of which I have been for years a most ardent advocate. To very positive arguments which might be adduced in its favor, are opposed mere negations by those who cannot accept it.

But the strongest arguments which can be adduced in favor of it must be those which experimentation or accurate clinical observation may afford. In this direction I would call your attention to the experimental results already reported from the Buffalo Laboratory by Dr. Gaylord, and especially to the photographs which I pass around showing the experimental results of Dr. Leo Loeb, who worked especially with small anir and particularly rats. It has peared more and more to the exp menters in this direction that ca can hardly be transmitted from mals of one species to those of anot but that it can be experiment transmitted from one animal to ano of the same species Dr. Loeb brilliantly demonstrated in the The photograph exhibited here is one of his experimental anim one of a large series in which he tr mitted the disease by intra-perito inoculation. The original tumor peared as a sarcoma in an an secured by him, and he has alr succeeded in producing the dis in from 200 to 300 animals of same species. This particular s men shows an intra-abdominal gr thus produced within a few weeks photographs being made by Dr. lord. (Dr. Loeb's paper, *Jou of Experimental Medicine*, 1 Such an unbroken series as this w seem to quite do away with all objections of the old line patholo as to failure in transmission of disease from animal to animal.

Contrast with this, again, photographs which I show you heart and liver from a patient w history, briefly, was as follows: patient was twenty-four years of and for a long time and up t death, under the observation of G. W. Wende of Buffalo, with w I repeatedly saw him. There i family history of any cancerous le He had a congenital pigmented on the shoulder, and in his occ tion was compelled to carry h firkins of lard, which he usually

n this shoulder, and by which he tantly irritated this little con- tal growth. He was noted for strength, and it was said of him he could lift a horse. By this ing he produced at this point an n sore which would not heal. At mœpathic hospital a ligature was around this growth so that it fell but it soon returned with a cluster rowths around it, some of which e pigmented and some not. One he photographs shows the appear- e of the back shortly after this dition was noted. (Fig. 2.) When seen by Dr. Wende he had be- en 200 and 400 pigmented and -pigmented small tumors of the scattered all over the body. When by me he was suffering from pnœa, and all the clinical evi- ces of mediastinal growth, and with every clinical evidence of nsive metastatic involvement of viscera. The *post-mortem* made by . Wende and Gaylord showed this e the case, and the heart and liver e in a condition indicated by the trations. Under the microscope picture was of rapidly growing inoma. (Figs. 3 and 4.)

Who can now view such a case as that fail to compare it with the most nsive and rapid spread of, for in- nce, tubercular disease? And who say, viewing either the slides or gross specimens that this sort of dition can be brought about by thing but an infectious agent?

Evidence of an entirely different racter is afforded by the study of alled "cancer houses" and of cases urring endemically, or in family ups. One of the best of recent dies of "cancer a deux," as the French call it, is that by Behla, who has already done so much in this line of investigation. (*Deutsch. Med. Wochschr.*, 1901, No. 26). He has here brought together a surprising number of cases of this kind, and of instances which stamp the disease as almost more than infectious, it appearing to be even in some instances actually contagious. From such sources and many others we can get ample justification for the statement made by Czerny that there is more reason for believing in the infectiousness of cancer than of leprosy. Additional argument against heredity of the disease can also be furnished by this statement that there is, so far as is known, not a single case on record of cancer in the new-born, and that it develops in human beings at a time when they are farthest removed from any hereditary influences.

Passing now from these aspects of the problem, let us consider some of its bio-chemical phases. Cellular morphology is far from being an exact science. There are minute differences between tumors which appear almost identical, and there are marked resemblances in tumors which appear very different from one another. No matter what the microscope may reveal, the clinician is quite able to affirm that most varying and variable conditions are obtained in different tumors. There is as much difference between cells of the same type and between their appearances as there is in shape between human noses. For instance, one case of epithelioma will proceed so exceedingly slowly as to become an affair of years' duration, while, at other times, its course may be so rapid as to stamp it as possessing the highest degree of malignancy. These

changes are not to be explained by the shape of cells nor character of surrounding tissue; they still constitute a part of the mystery of cancer.

Nevertheless, something of light has been shed upon these differences in cell growth by bio-chemical investigations, such as those made, for instance, by Brault (*Le Prognostic des Tumeurs base sur Glycogene*, Paris, 1899), which pertain to the amount of glycogen present in the tissues of certain tumors. In various papers he has shown the prognostic value attaching to such researches. All tumors, without exception, contain a certain proportion of glycogen, especially those of epithelial origin. This glycogen seems to be stored up as a sort of reservoir of potential energy, whose quantity is a measure of the possibility of rapid cell action.

It is a rather curious fact that while histology demonstrates certain fundamental differences between sarcoma and carcinoma, for instance, these differences are not maintained or cleared up by chemical activity of the cells which constitute the tumors. For instance, in sarcoma of a limb there may be present an enormous accumulation of glycogen, and this whether the cells assume the small, round, or the large spindle shape. Even in benign tumors glycogen is not lacking, for it has been observed in almost every one of them. This is important, for it would seem to show that glycogen is an index—not of malignancy, but of rapidity of growth, *i. e.*, as said above, of potential energy. The glycogenesis noted in tumor formation is not distinguished by any important peculiarity, for it proceeds normally in various parts of the body, as, for instance, the liver and the muscle. Tumors, like other parts of the body, are simply collections of cells, whose growth does not seem to follow such fixed laws, however, and which seem to have escaped from certain impulses. In sarcoma, for instance, the cells, though pushed to a certain distance from centers and deprived more or less of normal secretions, preserve nevertheless, the faculty of storing glycogen, no matter what their shape or size. Whether these tumors develop in the liver or at a distance there seems no difference in their glycogenic contents, nor does it matter whether, when in the liver, the biliary passages are closed or not. In fact, glycogenesis is simply a cell function and it is not the exclusive property of any particular organ, but is necessarily inseparable from the activity of tumor growths and cannot be localized. It is also worthy of note that the glycogen thus formed does not act, as though it were a secretion to be formed and used for a purpose, but is simply stored up, as it were, in a reservoir for use when needed. A careful bio-chemical study, therefore, of tumors will show that the glycogenic coefficients of their tissues are indices to the degree of their malignancy, or to the possibility of their rapid transformation.

The relations between inflammation and cancer formation seriously concerned the minds of the pathologists of the earlier part of this century and that preceding. For instance, Bruns, who described an inflammation of the rectum, which must have been malignant, died himself of the same trouble; and writers like James in 1706, Nisbet in 1795, Burns in 1800,

. ACUTE MILIARY CARCINOSIS. REGION OF PRIMARY INVOLVEMENT; BACK. DR. G. W. WENDE.

Wenzel in 1815, ascribed all tumor growths to an inflammatory origin; which was not strange under the conditions of knowledge obtaining at that time. Even comparatively recent writers have not been lacking who ascribe the lowering of tissue resistance to an increasing blood pressure, for instance, such as is seen in the ordinary chronic inflammatory disturbances.

The subtle influence which guides epithelial formation in a pretty uniform direction has been likened to that which makes crystals of the same substance assume invariable peculiarities. They form in obedience to some unknown influence, while epithelial cells form a cancer in obedience to some mysterious law with which we are not acquainted. Nevertheless, it is undeniable that the more cells a tumor contains within a given space, the more malignant are its clinical characteristics. Ackermann (*Hellin, Struma sarcomatosa*, München, 1893), for instance, has stated that sarcoma differs from fibroma merely in this respect—that the cells have not had time to complete their progressive metamorphosis into ordinary connective tissue. Certain it is that many normal tissues are built up from small beginnings, just as are the tumors; the thyroid, for instance, as Gegenbaur has reminded us, which grows like a neoplasm. It is a growth which differentiates itself from embryonal tissue in the most significant way, and I have seen at least one case, myself, in which it seems to have continued to develop into a mass which became a tumor, and determined the death of the child. In fact, the various metamorphoses of embryonal tissue almost defy scrutiny and classification. The cells of a lipoma, for instance, undergo a cert change which reminds one of emb onal tissue before they enter into composition of a distinct tumor. M oma is almost an intermediate st between lipoma and sarcoma and can often follow the changes as follows the tissues from benign i malignant alterations. In fact, acc ing to Virchow, it is in one sense incompleteness of a given tissue wh furnishes excuse for development c tumor in the same. This is, perha especially true of nævi. The m complicated the structure of the or inal tissue the greater the danger tumor formation. The simplicity muscle cells and of true nerve c constitutes their exemption from t tumor formation, since we have no t tumor forms of striped muscle, nor nerve cells. Not very different is c cinoma of organs or parts undergo retrogressive metamorphosis.

Many of these changes remind also of changes that go on norma in the young tissues; carcinoma forn tion of the skin glands, for instan is almost the same process as that which the epithelium grows downwa and first forms them. Epithelial c penetrate as a solid column, wh undergoes a certain liquefaction t corresponds to the softening going in many cancers. Cancer cells see in some cases, "born" too early, a in some cases, too late. The occ rence of truly embryonal cells in ad tissue is physiologically an anachr ism which some medical philosoph have been pleased to record as a sort atavism. That which in normal t sues is transitory, in cancer rema stationary. Carcinomatous tissue heterologous only in the develo

ıtal sense, not when the embryo is sidered. Cancer cells resemble the emeral insects which appear, pair mselves, reproduce their kind, and all in the same day. There is much he nature of cancer cells to put us ously in mind of some atavistic cess. The cells lose their function l develop wildly. Nor should we get these peculiarities which evince mselves when cells intended for one pose assume another function. us, for instance, in complete pro- se of the uterus, where the mucosa closely resembles the skin, we may that a naturally concealed and p lying tissue has appropriated the culiarities of the superficial tissue. is the most indifferent tissues which ve the most common points from ich a new growth takes its origin as cancer of the eye, for instance, since m the peculiarly specialized parts the globe cancer rarely arises.

Hellin sums up his views on cancer mation with this rather significant nt; the therapy of cancer must prac- ally be an effort to prolong the dura- n of life of cells. To lower their mperature, to shut off their fluid pplies, would seem, according to him, e primary indications.

In an interesting biological study garding cancer, Hellin (*Das Carcinom; ne biologische Skizze*, Leipzig, 1898), arts out with this general statement hich, of course, will find general ac- ptance, that between the duration of e and fecundity of a given animal or getable organism there is always quite constant relation. This axiom tains not merely for different species animals, but also even for individual lls of both kingdoms. He makes it pear, moreover, that the natural lifetime of a cancer cell is brief; hence, its extra activity, its tendency to rapid cell division, all of which are in obedience to this law. The more cells a cancer contains the more malignant it is, while it is universally accepted that the most malignant cancers are those which have the smallest cells, and that an increase in size of component cells gives less rapidity of cell division and diminished malignancy. This short but strenuous life of cancer cells would seem to be determined by external or internal irritation—irritation, that is, in the sense of some extrinsic influence which affects its activity. Such influences, for instance, are the heat which hatches an egg, the warmth and moisture which effect the germination of seed, etc. When such external agency acts continuously, then we may speak of its effect as a chronic irritation and expect constant results. Among such irritations trauma has always been regarded as constituting perhaps the most important, or at least the most demonstrable, but mechanical injury is only one phase of the general subject of irritation from without, which should be made also to include temperature changes, the influences of chemical activity, etc. Cancer of the stomach, for instance, which is perhaps the most frequent of all varieties, occurs where irritation is most constant and if we seek for those other parts of the body where cancer is most constant we find them about the uterus, the breast, the rectum and intestines and the face. In other words, in those positions which are most exposed to direct infection, or other irritation. We see the influence of dirt upon the skin, for instance, in cancer of the face in the lower classes, in cancer of the lip,

in paraffine cancer, chimney sweepers' cancer, etc. These points of predilection are not merely those exceedingly exposed, but are those also where regeneration occurs least kindly, *i. e.*, at points where the skin and mucous membrane meet, because along these lines there is a variation in the type of cell structure. The only apparent exception is, perhaps, in the liver, which is still known to be an organ exceedingly capable of regeneration, and which is rarely the seat of primary cancer. This is due, probably, not so much to its functional peculiarities as to its protected position, and yet, even here we know what the irritation of gallstones may produce.

We have not yet learned what the mysterious influence is which, in most cases, controlsthe size and shape of a growing mass and converts it into an organ or a part of one type or another. We may call it polarity, or call it what we will. At all events, we cannot refuse to recognize it. In cancerous growths it would seem as if this particular influence were lacking or had not made itself completely felt, because in cancer there seems to be absolutely no regulation of the process of cell growth which proceeds widely and without purpose, following only the mechanical law of growth in the direction of least resistance.

It is interesting that observers like Hellin, who find little to commend in the parasitic theory of cancer, nevertheless cannot explain the rapid cell growth of tumor formations without invoking the hypothesis of some mysterious irritation. The Germans, for instance, are always talking about "chronischer Reiz," and, at the same time, explaining nothing of the statements and demonstrations of othe with regard to the decided parasit nature of this *Reiz*. It is an easy thi to state with a certain pompousness expression that increase of cells in cancer is due to their relatively stren ous and shortened lives, which is to accounted for by the persistence of chronic or intermittent irritation. Th explains nothing and should not be a cepted as of much value. It is a stat ment, however, which probably no o will challenge, but it leads us to se further for the nature of this alleg irritation; for which no adequate e planation has been offered, as comi from the cells themselves, and whi can only be conceived of as an eleme intruded from without. The c growth cannot go on indefinitely a eternally, and so comes necessarily end, which is the breaking down of t cancer itself. The more active t growth, the quicker its end is attain Even crystals by the rapid or sl deposition of the molecules which fo them do not grow forever, and th comes an end to the formation of ev crystal, no matter how favorable surroundings for crystalline formati Cell division is in some respects expression of a struggle for existen which is determined by a lack of s ficient nutrition. When nutrition plentiful, cells attain larger size a labor less strenuously. When nut tion fails, individual enterprise m be increased. At least, this seems be the law of cell growth. This helped to a certain extent by favora temperature conditions. Increased activity leads to increase of h and each influence seems to act u the other. A third favorable con tion is access of water, which seems

FIG. 3. ACUTE MILIARY CARCINOSIS; HEART. DR. WENDE.

be an absolute necessity to animal and vegetable life. The embryo, for instance, is made up of about 87 per cent. of water, whereas adult tissues contain about 70 per cent. The same variations are seen between young and old plants. They obtain, moreover, between different portions of the same organism. In the growing tree the most rapid alterations are seen in those parts which are most moist, whereas in the thick and almost dried substance of the woody fiber, changes are much less rapid. It would seem as if the malignancy of a tumor could almost be made out by its juiciness. Certain it is that the most rapid growths are the softest and most succulent. This fact seems to have been made quite clear by Kahane (*Centralblt. fur path. Anat.*, 1895, p. 673), and Beneke has emphasized how often individuals loaded with œdematous fat tissue succumb to cancer.

The reciprocal relations of cancer and tuberculosis have been the subject of very lively discussion for the past twenty years, one side holding with Hunter and Rokitansky to an actual antagonism between the two diseases, the other with Lebert, Weber and others that their coexistence amounts almost, in some instances, to a symbiosis. It was in 1879 that Picot (*Gaz. Hebdom.*, 1879) published a most complete report of a case of cancer of the liver, in which there existed, at the same time, large tubercular cavities in both lungs. This was, to be sure, before the acceptance of Koch's views and his description of the bacilli of tuberculosis. The coexistence of the two diseases is an actual fact, while those lesions which most interest the surgeon abound in regions where mucous membrane and skin come together, but i especially those particular lesi where both diseases appear in cl proximity, or involve the same ar that most interest us. To be sure, t is almost equally true of syphilis a cancer, for the development of epit lioma upon a syphilitic basis is alm as common as upon a tubercul Cruveilhier reported, in his time, to Anatomical Society a case of so-cal areolar sarcocele, which he descrit as both cancerous and tuberculous. will be worth while to take a little ti and with Claude (*Cancer et Tubercul* Paris, 1900) discuss these relatio first, the development of cancer upo tuberculosis basis, and second, the velopment of tuberculosis upon a ca cerous basis.

It has been a well-known fact some time that lupus is frequently f lowed by epithelioma. This was, p haps, first insisted upon by Devergie in 1854. When this transformati occurs, the disease rapidly spreads, t neighboring lymphatics become i volved, and the lesion itself becom much more painful than previous was the case. The most careful rece study of this morbid condition has be made by Desbonnets (*Epithelioma Lupus. These de Paris*, 1894). Wh this transformation occurs it may ta place over a portion of an old lup area which has become cicatrized, upon the fresh active portion of its su face. Twenty-one times out of nine Desbonnets saw a cancer appear upon cicatrized lupus area. The subject h been studied in Germany, especially b Busch, who described, in 1872, what now generally known as lupus ca cinoma. According to Busch this a fection is particularly common upo

e extremities, and is often coexistent th other tubercular lesions. The rticular cases of lupus most likely to ndergo this change appear in the form papillomatous ulceration which bemes cracked and fissured easily, but hich yield readily to treatment by the harp spoon. This has been called by hutz papillomatous lupus.

In 1890 Garre published one of the rst cases of lupus of the larynx undergoing cancerous degeneration. (*Beit. lin. Chir.* III.). Baumgarten and rone studied other combinations of he two diseases about the mucous surace of the larynx, and in 1891 Zenker eported two quite classical cases of his character. In the first of them here was ulceration of the œsophagus, f epitheliomatous type. At the borler of this ulcer it was easy to make out he presence of miliary tubercles in arious stages of evolution, while within little distance the mucous glands were in a stage of well-marked epitheiomatous proliferation. His second case concerned a tumor of the vocal cords, which proved to be typical epithelioma, while, along in close contact with it, were unmistakable foci of tubercular disease containing bacilli.

In pulmonary consumption, cancerous neoplasms have been repeatedly observed in connection with the tubercular lesions. Thus Friedlander has described a pavement epithelioma, with pearly bodies involving a lung cavity. (*Fortschrift. d. med.*, 1885, No. 10.) Menetrier thinks that the sclerosed tissue around such a cavity constitutes particularly favorable soil for the development of a primary epithelioma. Schawlbe has also reported a similar case of cancer, developed in the wall of a lung cavern. (*Virchow's Archiv.* Vol. 149, p. 329.) The consideration of questions like these has led Ribbert to raise the question whether the disorganization of epithelial arrangement produced by the tubercular lesion may not be the exciting cause of the epithelial proliferation.

With Crone and Zenker, one must admit that the tuberculous process is at least capable of acting as an irritation which, like any other continued irritation, may provoke epithelioma, while at the same time it probably also lowers local tissue resistance. Warthin has reported somewhat recently a striking case, which is as follows (*American Journal Medical Science*, July, 1899): a woman of forty could not nurse her eleven-month-old baby, because on the right side was no milk, and because the left breast was painful and the nipple retracted. In this breast pain increased and a small tumor, hard and tender, appeared, which grew rapidly with axillary adenopathy. Exploratory puncture returned pus, containing tubercle bacilli. Subsequent operation revealed the presence of a number of tubercular nodules in various stages of degeneration, while at the same time there was a very distinct epitheliomatous formation in the connective tissue stroma, and around the nipple and the lymph spaces. The reporter considered that the tubercular process preceded the cancerous. He also reports a second case of a cancer of the breast associated with tuberculosis; in this case the tuberculosis appearing to be the second in the order of precedence.

Dufour (*Bull. de la Soc. Anat.*, February, 1898), has studied an endothelioma which he thought to be of arachnoidal origin, which lay in con-

tact with a focus of tuberculous ostitis at the lower end of the spinal column. The tumor did not appear to be infiltrated by tubercle, but inoculation gave a positive result, which could only be attributed to the presence of bacilli penetrating from the neighboring tubercular focus. Ribbert believes that the rarity of cancer transformation of visceral tubercular lesions is due to the rapid caseation which tubercular foci so placed undergo, the conditions being different from those obtaining in lupus of the skin, etc.

Lubarsch (*Virchow's Archiv*, III., p. 281) studied carefully the reports of autopsies in the Pathological Institute at Breslau for a period of twelve years. His analysis of 6,536 reports shows that 2,668 (*i. e.*, 41 per cent.) died of tuberculosis, and 569 (*i. e.*, nearly 9 per cent.) died of cancer. Of the 2,668 tubercular patients, 117 (4-10 per cent.), were cancerous. Of the 3,868 non-tubercular patients, 452 (117-10 per cent.) were cancerous. Of the 569 cancerous patients, to reverse the figures, 117 (20 per cent.) were tubercular, and of the 5,967 non-cancerous patients 2,251 (42 7-10 per cent.) were tuberculous. These figures will give a general idea of the relative frequency of the coexistence of these two diseases: that is, that in a general way, from 4 to 5 per cent. of tubercular patients suffer also from cancer, while about 20 per cent. of cancerous patients suffer from tuberculosis. The figures of Lubarsch have been fairly confirmed by results obtained elsewhere by Zenker, Cordua and Loeb.

The two diseases may be met with together, under the following conditions: (*a*) Independent co-existence where neither one seems to be in any way related to the other; (*b*) M tastatic cancer developed upon old or recent tubercular lesion; Primary cancer actively appearing a secondary infection; (*d*) Chronic bercular lesion developing upon near a cancer; (*e*) Simultaneous velopment evincing almost a sy biosis.

The term cancer in this connect should be understood in its in comprehensive significance imply more than mere epithelioma, thou the latter is the most common of th manifestations in connection with bercle. Iscovesco (*Bulletin de la S Anat.*, 1888) reported to the Ana mical Society of Paris, in 1888, case of sarcoma of the lung, simulati phthisis, where there were most d tinct sarcomatous nodules in t pleura, with infiltration of the ba of the lung, existing along with e tensive tubercular cavities and a co plete series of distinct disseminat tubercular granulations. Reich (*A beit. a. d. path. Inst. zu Gotting* 1893, p. 167) has reported a cereb tumor composed of a combination glioma and tuberculoma. Cleme (*Virchow's Archiv., Bd.* 139, 189 has reported an endothelioma of t submaxillary region, complicated wi tuberculosis. It occurred in a wom of fifty-two, and recurred after t first operation, so that a second atta was made upon it. Portions remov at this time gave the picture of e dothelioma only, whereas the fi specimen was distinctly tuberculo as well. Clement has also report other cases; for instance, cancer the lower jaw, with tuberculosis of t cervical lymphatics; another of canc of the breast, with tuberculosis of t

FIG. 4. ACUTE MILIARY CARCINOSIS; LIVER. DR. WENDE.

axillary lymphatics; and another of cancer of the stomach, with ulceration of the mucosa, and, at the same time, distinct tuberculosis of the mesenteric lymphatics, and of the liver, without any trace of metastasis in these latter structures. Crawford (*Lancet*, 1892, p. 195) has described a scirrhus of the breast in which there was an abscess. In the tumor itself there were neither bacilli nor giant cells, but the axillary lymphatics were distinctly tubercular. I have myself recently treated a case of epithelioma of the palate, accompanied and followed by tuberculosis of the cervical lymphatics on both sides.

On the other hand, numerous observers have reported cases of tubercular lymph nodes transformed into malignant lymphoma. Askanazy (*Ziegler's Beitr. zur. Path. Anat.* III, p. 411), and Cordua (*Arbeit, a. d. Path. Inst. zu. Gottingen*, 1893) have both reported instances of this character where tumors have recurred after operation and have finally led to the death of the patient. I have myself seen within the past year and a half at least two cases where this combination seemed to me extremely evident, although in neither instance was I able to follow them up in such a way as to permit of a careful report which might positively establish the statement.

Ricker (*Archiv. fur. klinische Chirurgie*, Vol. 50, 1895.) has reported the following most suggestive instance: A boy of fifteen, who had for many years voluminous tumors upon the lateral region of the neck, was operated in 1890. Four years later another operation was undertaken because of a new collection of masses in the same region, but was found be so difficult that it was not f completed. Section showed a tinct type of malignant lympho The lad soon began to run down, tumors of the neck became adhe and ulcerated, other similar for tions appeared, and the patient fin succumbed with paraplegia. At autopsy lesions were found in the n in the thorax, around the bronchi the lungs, in the adrenals, and the vertebral canal. At this la point, the lesions seemed to amo to those of a generalized lympho comatosis. While this diagnosis co be made with a microscope with doubt, it was found at the same t that there was advanced tubercu disease in the neck, with caseati Dietrich (*Beit. zur. klin. Chir.*, X 1896) and Fischer (*Archiv. fur. k Chir.*, 1897, Vol. 55) have also ported very characteristic cases which the association of malign lymphoma and tuberculosis was dent; thus Fischer reports twe patients, of whom four died. Fre weiler (*Arch. fur. klin. Med.*, 18 also has described recently an asso tion between lymphomatous lesi and lymphatic tuberculosis. I h seen the same association of disease a girl of ten.

Müller is quoted by Ricker to following effect: A woman was op ated on for tumor of the breast, c sidered sarcoma, which, however, w not subjected to a microscopic stu The operation was incomplete, a two years later there were found in t breast two distinct tumors, one t size of an apple, the other the size o pigeon's egg. The patient seemed be affected with a general sarcom

is. The former of these two tumors sented all the characteristics of a ical lympho-sarcoma. The lat- contained distinct evidences of seminated tubercle, and within its erior a distinct caseated mass, und which tubercular bacilli were ily found.

Tubercular infection complicating an eady present tumor is probably least known of the various pro- ses here reported. There is no estion, however, but that tubercle cilli may penetrate into a cancerous wth and give rise there to tubercu- foci, which latter may undergo the linary changes common to such ions in other parts of the body. umgarten and Crone (*Arbeit. a. d. th. Inst. zu. Tubingen* Bd. II.) re- rt, for instance, the following: A man of forty-four, operated on for small papilloma of the larynx, which en examined was found to be a all epithelioma. Some months later recurred, tracheotomy was done, d the examination of portions of e tumor revealed the presence of dis- ct tubercular granulations. This was lowed by extirpation of the larynx, which careful study showed a com- nation of cancer and tuberculosis, e same association being found in e lymphatics of the neck. Baum- rten, moreover, has observed about e same combination in a case of ncer of the rectum which was com- icated by most evident tubercular anulations in the cancerous tissue. riedländer (*Virchow's Archiv.* Vol.) has briefly reported the details of case of cancer of the stomach, devel- ed upon the base of a round ulcer, hich base was surrounded with tuber- losis. Cordua (*Arbeit. a. d. Path. st. zu Göttingen*, 1893, p. 147) studied a cancer of the œsophagus secondarily infected with bacilli, and came to the conclusion that the cancerous surface served as a point of least resistance and was attacked accordingly by the bacilli. Claude (*Cancer et Tuberculose*, Paris, 1900 p. 64) has reported the instance of a man of sixty-one entering hospital with an intense diarrhœa which had lasted for four months, and who at the same time had most marked cachexia. The autopsy showed extensive tubercular lesions of the large intestine, the lungs were also involved, while in the stomach a large cancerous tumor was found, surrounded by distinctly tubercular lesions. Evidently a portion of the tumor itself was breaking down with tubercular ulceration.

The following instance, illustrative of the close relation between injury and cancer growth, is reported by Steinhaus in a recent Polish journal (*Medycyna*, 1900 No. 47). A woman of forty applied a blister to her forehead on account of headache. As a result of this, there formed an ulcer which would not heal, and in spite of constant treatment, suppurated and discharged for five months. After that length of time the base of borders were excised and the defect filled by Thiersch grafts. After a few weeks, ulceration began at the point of operation and the Thiersch grafts were once more tried. Microscopic examination of the excised fragments showed the borders of the ulcer to have become cancerous. The case seems the more interesting as showing the peculiar effect of a chemical irritation applied for but a short time, since it is usually only long continued irritation which provokes cancerous growths.

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