SOME NOTES ON CANCER
WITH SPECIAL REFERENCE TO THE PARASITIC THEORY*

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From all the uncertainties that still surround the problem of cancer, there stands out at least one observation which, by general agreement, has been universally accepted as a definitely established fact: that the cancer cell was at one time a normal tissue cell, a cell of that particular tissue in which the cancer arises (1).

On analysis this statement reveals two phases in the life of the cancer cell; first, the period of change in which the cell is transformed from the normal to the cancerous state; second, the period after the completed transformation: in other words, the periods of genesis and of perpetuation of the cancer cell, or, as they are also called, the precancerous period and the cancerous state proper (2).

Cancer research has in the past been principally concerned with the second phase. Tissue already cancerous was used in the experimentation. By transplanting such cancerous tissue artificial metastases were produced and were then made the objects of study.

Through the literature of all those years runs the longing for the time when experimental attack on the first phase of the cancer cell should become possible. That time is now at hand: Primary cancer is actually being produced experimentally—"carcinoma is produced at will, at any time, in any quantity" (3). A new day has dawned in cancer research. A giant step forward has been made.

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The methods employed in the artificial production of primary carcinoma are quite numerous. They all start from the normal tissue. The chemical method is the one which has been most used thus far. Coal-tar or the fractionated derivatives of coal-tar (4), also wood-tar, has been brushed for months at regular intervals upon the ears of rabbits (5) or the backs of mice (6) and under this treatment the affected normal tissue cells gradually undergo changes. After a while benign growth sets in, and this benign growth eventually becomes malignant. The whole process of the development of a primary carcinoma, from start to finish, can now be watched day by day in its progress, macroscopically and microscopically, and the observation can be repeated ad libitum.

Next in importance, because also exposed to view, stands the previously uncontrollable X-ray cancer. Through recent discoveries in dosage it is in a fair way of becoming an exact experiment.

The remaining methods, parasitic and mechanical, for the artificial production of cancerous growths yield more or less inaccessible and, therefore, not so readily observable tumors. A very large amount of work has already been done along these lines of investigation (7). Cockroaches have been infected with nematodes and on feeding these cockroaches to rats the surviving rats develop chronic gastric lesions and some of them cancer of the stomach. Similar experiments have been made on frogs (8).

Mechanical means also have been tried with success. Rats were fed with oats (9), also with barley (10). The bristles carried by the individual grains stuck in the tongues and between the teeth of the animals and in some instances cancer of the tongue made its appearance.

The largest number of artificial tumors have been produced by the method of Bullock and Curtis (See J. Cancer Res., 1924, viii, 1), which consists in feeding rats with cat excrement containing ova of Cysticercus fasciolaris. More than a thousand sarcomata of the liver have been thus produced.
The foregoing will suffice to support the statement that we are now in the epoch of experimentation on primary carcinoma, produced at will and developing and growing under our eyes. Cancer research has entered into a new era!

In the clinician these great achievements of the laboratory kindle anew the hope—so often and so eloquently expressed by surgeons, but never fulfilled—that they may lead to the discovery of a method that will make possible the diagnosis of internal cancers before they become palpable, when they are only too frequently already inoperable. Such a clinically practical method is most urgently needed. As yet cancer carriers, the same as typhoid carriers, apparently in good health, may go undetected for a considerable time, either because their condition does not give them enough trouble to make them go to the doctor, or if they do go, because their symptoms are so slight that the seriousness of their condition is not suspected (11). Even under the painstaking health control of soldiers during the War, there are on record two cases of men who had done service until shortly before they were found by exploration to be suffering from inoperable cancer of the stomach (12). Not infrequently cancers are found at autopsy, which during life produced no symptoms, yet had already metastasized into other organs (13). Quite recent hospital statistics of the University of Breslau show that of the cases of carcinoma of the rectum admitted to the clinic, from 60 to 70 per cent had not been diagnosed before admission (14). Of the 15,000 cases of carcinoma uteri which annually occur in Germany, from 30 to 40 per cent are inoperable when they come to treatment (15). Other statistics also show startling results. Of 700 deaths from cancer of internal organs in German hospitals, the condition had not been diagnosed during life in 28 per cent of the cases; of 4,300 British Hospital cases, in 40 per cent (16). Surely such figures speak an impressive language, even though the last are not recent ones. They strongly emphasize the necessity of extending the newly opened avenues of research into this field.

Commendable beginnings in that direction have already been made. It has been shown that red blood corpuscles, which con-
tain normally 12 to 15 milligrams of phosphorus in 100 cubic centimeters, contain 18 to 20 milligrams in cancer patients (17); also that the curve representing the results of the sugar-tolerance test of cancer patients has characteristic peculiarities (18). Chemists have been quite active in this field. But the methods they suggest do no more than give us a warning always to suspect cancer. However, we need something more definite and this, I hope, will come if the cancer research laboratories also bend their energies to the task. A method enabling early diagnosis of internal cancers ought to be one of the practical results of observation on and experimentation with primary carcinoma in statu nascendi.

There is another hope attached to such experimentation; namely, that it will unite in one camp all those who are interested in cancer research. Thus far there have been—or, to be accurate, it may perhaps be said, there still are—two camps, more or less antagonistic from a scientific point of view, the one comprising adherents of the cellular theory, the other, counting a number of surgeons among its followers, the searchers for a specific parasite.

In years past I, also, belonged to the contingent of surgeons who believe in a specific agent of cancer, and hoped it would ultimately be found. Conditions in the latter part of the last century were especially favorable to the fostering of such expectations; it was a time when the discovery of the specific agents of many diseases was the overshadowing event in medicine. We knew then not quite so much of cancer as we do now, and the demonstration of its specific agent appeared in those days not only plausible but also most desirable, because seemingly it would have simplified matters.

Moreover, surgeons gravitated naturally to such an expectation by reason of the many instances in which they came upon cases of the most rapid development of numberless metastatic foci, e.g., in miliary carcinosis of the peritoneal cavity where, macroscopically, the symptoms make it next to impossible to regard the condition as other than infectious (19). Such experiences made them rather tenacious of their standpoint. But
something happened that set me thinking. Ten years ago, when Aschoff was here, I asked him whether he shared Klemperer's (20) just then publicly expressed hope for the ultimate discovery of the specific cancer agent. He replied: "And if you should reach Methuselah's age, you would not have lived long enough to see that happen." Frequently that remark came back to my mind, and I determined upon a broader study of the literature. In that study I have been engaged in recent years, and it has converted me to views regarding the etiology of cancer which, I believe, coincide more closely with the ideas entertained at present by research workers, and which I have adopted the more readily since the production of primary carcinoma by non-specific means seems to have placed a final quietus upon the specific theory. The further discussion of the latter has hereby been rendered rather academic. Yet it may not be amiss to consider very briefly and without going anew over much debated ground, just where the case stood before the laboratory succeeded with the experimental production of primary carcinoma and to obtain thereby, incidentally, some sidelights on the etiology of cancer.

It should perhaps be stated at this point that in this paper the term "cancer" is used in the laboratory sense to cover all malignant growths, and not in the clinical sense which makes cancer and carcinoma interchangeable expressions in contradistinction to sarcoma.

The question as to the etiology of cancer may be framed thus: What pathogenic cause limited to vertebrates—for true cancer occurs only in them—is common to humankind of different races and climate, to dogs, horses, cattle, mice, birds, and fish, to wild and domestic animals, herbivora, carnivora, and omnivora? "It can hardly be a specific infecting agent, for there is not in existence a known microbe so indifferent to the choice of its host as to be capable of infecting all these beings" (21). At the time the foregoing was written diligent search had been made for the specific cancer agent for decades. But the frontal attack bringing no result, indirect means of proving the presence of such an agent were resorted to, and stress was laid on statis-
tics. Forty-five thousand cases, compiled under Czerny's direction (22), covering the years 1883 to 1907, disclosed marked regional diversity of cancer incidence for Baden, some parts of it having had no cases at all, others showing figures considerably in excess of the average. The state being small and there being no climatic, economic, or other pronounced differences between the several sections except as to cancer incidence, Czerny argued that there must be a *contagium vivum* in either the people or the soil and, as the people were moving freely from place to place, that it must be in the soil. Similar deductions were made in England from investigations (23) which seemed to show that regions with rock foundation had a smaller cancer incidence than alluvial river bottoms with clay subsoil. Many other investigations were made on similar lines, but in smaller districts, with the result that to cancer regions were added cancer towns, cancer streets, cancer houses, and even cancer rooms.

We are thus confronted with the question: What justification is there for such deductions from the collected data. To this question Michaelis gives the answer: "Conceding the correctness of the statistics, they point to a common source, but prove nothing for the contagiousness of cancer" (24).

Can this dictum perhaps be supported by observations bearing the character of experiments on a large scale? Observations on the shores of the Baltic and in Siberia appear here in point (25). Attention had been directed to the prevalence in those neighborhoods of cancer of the gall-bladder among certain fishing crews who spent most of their time aboard certain boats. According to the old explanation, the cry of "cancer boats" would probably have been raised, and no effort would have been spared to search the boats from stem to stern for the *contagium vivum*. As a matter of fact, the boats were quite innocent of the occurrence. Investigation disclosed that it was the habit of these men to eat raw fish while out cruising, and the fish were found infested with the larvae of trematodes, helminths. In the same way as Fibiger's rats were infested with nematodes (which are also helminths) by feeding them on nematode-infested cock-
roaches, so these eaters of raw fish had been infested with the
trematodes found in the fish.

Now it is a curious fact that the several kinds of helminths
have a predilection for various organs of the human body; the
Distomum haematobium (26) of the Bilharzia for the portal vein,
traveling thence upstream by way of the veins to the bladder
and to the rectum; the Schistosomum japonicum (27) for the
colon; the Cysticercus fasciolaris (28) for the liver; the Spiro-
ptera neoplastica (29) for the stomach, and the Opistorchis felineus
(25), the trematode here in question, for the gall-bladder. Thus
it happened that the gall-bladder and the bile ducts of these fish-
eaters contained anywhere from a few to a thousand worms. The
lateral pressure exerted by the worms and the numerous ova de-
posited by them in the gall bladder and in the bile-ducts of the
liver, caused therein chronic inflammation which led in due course
in some of the cases to the onset of carcinoma, preceded in the
liver by cirrhosis. From an exact experiment the foregoing obser-
vation differs only in so far as the men had not been requested by
an investigator to eat infested fish, the common source, but had
done so of their own volition.

Another observation (30) here in point has been made on the
coast of Norway, where in a settlement of some 3400 souls, com-
pletely isolated by mountains and deep-cut fjords, families live
closely packed in one-room cottages. Yet, with every chance
for contagion present, if there were cancer contagion, the cancer
incidence over a period of 22 years was nevertheless among those
above 35 years of age no more than the world average, about 9
per cent, except only in four of these families in which it
amounted to about 20 per cent. In one such family the father
and the mother had cancer. All their children but one emi-
grated. The stay-at-home child nursed the parents and de-
veloped cancer; the emigrants remained immune. Here the
cancer house and its contagion seem to appear also with the
exactness of an experiment. But is not the "house" as innocent
of the occurrence as the "boat" was above? May not these
fisher-folk also have been eaters of raw fish? Or may not infec-
tion with parasites through vermin have come into play? It
requires no great stretch of the imagination to suppose that the cottages of the four families were located where water-rats abound; nor would it, after the experiences in the last war, appear improbable that these people, considering their mode of living, had fleas or lice or bed-bugs. We are told that Morau (31), the pioneer of large-scale systematic cancer transplantation in mice, transferred bed-bugs from the cages of cancerous mice to those of healthy mice, whereupon a large number of the latter developed cancer (32). We also know that rodents almost without exception are infested with helminths (33), cestodes and nematodes; and we further know that bed-bugs, fleas, and lice, on feeding upon such rodents absorb with the blood the larvae of helminths. When, later on, the insect inserts its proboscis into a new victim for another feeding, there is a strong outflow of the insect's saliva through its suction tube, the saliva having qualities that prevent blood coagulation, thus keeping the tube open, and with the outflowing saliva are given off the previously absorbed larvae into the animal on which the insect feeds. Extensive researches were made into these matters during and prior to the War (34). Thus there would appear to be a possibility that the Norwegians, if not by eating raw fish, became infested through the stings of intermediate insect hosts, and that by way of this route from a common source cancer developed separately in each individual without reference to the other and without contagion.

Still another case in point is presented by the studies on cancer incidence among the natives of Norderney, a small summer resort island in the North Sea, made up of sand dunes with a village of fisherfolk at one end, old residents all of them (35). In 20 years there had been 31 deaths from carcinoma, 16 of them in eight adjoining houses in a small district; and in five of these houses had occurred in all 13 cases; in one house 5 cases. All these houses were found located in the lower part of the village, the so-called "garden town," having water in their cellars at high tide. In 1897, of a total of 5 cases, 4 occurred in this particular part of the village within four months. It will at once be noted that conditions here are ideal for the presence of water
Moreover, the name "garden-town" brings to mind observations in Luckau (36) where, in the various districts of the town the cancer incidence was from 1 in 20 to about 1 in 30 deaths, but in one suburb, a garden-town, 1 in 9. Commenting (37) on these and other related observations, writers have ascribed the greater frequency of deaths from cancer in such localities to the "eating of raw vegetables growing in soil fertilized with night-soil or with barnyard manure"; and the opinion is further expressed that "there are many facts which seem to point to sewage and manure as the home of the organism causing cancer." All of this may be correct, provided the reservation is made that the parasites, which may enter the human system in that manner, are non-specific.

By the above assumption light would also seem to be thrown on the very puzzling high cancer incidence of the city of Berlin. Recent statistics (38) of the Swiss Cancer Research Committee show the following number of cancer deaths figured per 100,000 of population:

<table>
<thead>
<tr>
<th>City</th>
<th>Cancer Deaths per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>New York</td>
<td>63</td>
</tr>
<tr>
<td>London</td>
<td>68</td>
</tr>
<tr>
<td>Edinburgh</td>
<td>93</td>
</tr>
<tr>
<td>Zurich</td>
<td>110</td>
</tr>
<tr>
<td>Paris</td>
<td>118</td>
</tr>
<tr>
<td>Berlin</td>
<td>165</td>
</tr>
<tr>
<td>Hamburg</td>
<td>101</td>
</tr>
</tbody>
</table>

Corrections may be necessary for the age distribution of the population of these cities but the figures are nevertheless interesting.

The mortality from cancer in Berlin per 100,000 of population from 1881 to 1910 increased as follows (39):

<table>
<thead>
<tr>
<th>Year</th>
<th>Cancer Deaths per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1881-1885</td>
<td>69.4</td>
</tr>
<tr>
<td>1886-1890</td>
<td>78.2</td>
</tr>
<tr>
<td>1891-1895</td>
<td>87.7</td>
</tr>
<tr>
<td>1896-1900</td>
<td>104.0</td>
</tr>
<tr>
<td>1901-1905</td>
<td>119.2</td>
</tr>
<tr>
<td>1906-1910</td>
<td>130.7</td>
</tr>
</tbody>
</table>

The sewage disposal system of Berlin, installed in the seventies of the last century, consists of a pipe system which carries the sewage to deep caissons, whence it is pumped to distant tanks and used in the irrigation of extensive truck farms; the vegetables raised there are marketed in Berlin. Proved high cancer incidence and proved consumption of lettuce, radishes, celery,
onions, etc., eaten raw and coming from fields fertilized with human sewage, stand here side by side. Speaking of non-specific parasites, Orth recently remarked (40): "Quite likely parasites are with much greater frequency than heretofore suspected an inciting factor in cancer development." The relation of sewage disposal to cancer incidence in Berlin might, though only under the above assumptions, properly be called an experiment on a large scale in producing primary cancer, with the truck farm as the common source.

A cancer district combining rats, gardening, sewage and a fourth factor—polluted well water—has been found in France. The town of Solesmes, on the Selle river, is bisected by a narrow, deep-cut stream, an affluent of the Selle. The water of this affluent is deflected into a mill race which runs along the hillside through gardens. Both the old stream-bed and the mill-race serve as open sewers; they disappear frequently below stables, houses, and streets. The island between them is overrun with rats. Wells on the island are sunk to the level of the stream-bed; the water in them is bad. The island is a veritable cancer nest. It is inhabited by the patricians of the town, a sturdy race, many living to a high old age. Of 91 deaths from cancer within ten years 85 occurred on, or were traceable to, the island, the poorer working class people living on higher ground contributing but six cases. Conditions were found reversed in the villages above and below Solesmes where the poorer people live in the swampy and annually overflowed river bottoms. Here the poor were the sufferers from cancer, and though tuberculosis was prevalent among them and many died below cancer age, yet the cancer incidence was very high, being in 10 and 12 years in the investigated villages respectively 5, 6, 8, 10, 12, 13, 17, and 21 per cent of the total number of deaths. In all of these villages rats were found present in such numbers as to constitute a real plague. Ascarides were of regular occurrence throughout the population of the district. In adjoining parallel valleys, only a few miles distant, inhabited by the same type of people, the cancer incidence was but 1 and 2 per cent of all the deaths. The investigator (41) contents himself with hinting at possible
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external influences in the causation of cancer. His facts seem to lend support to the surmise advanced above regarding the rôle of helminths in the causation of cancer. As the rats were swarming everywhere, their excrements probably contributed to the pollution of the well-water. Rat excrement carries the eggs of helminths in large quantity (42). By use of the well-water and of the diluted sewage of the mill-race in the watering of the gardens, and by fertilizing the soil, as is customary there, with human and stable manure, helminth eggs were probably brought to vegetables which, eaten raw, became a source of infection to their cultivators, a circulus vitiosus.

Ascaris lumbricoides (43), regularly found by Borrel in the carcinoma of mice (44), emigrates from the intestinal tract into the gall-bladder and the liver, with the consequences noted above for Opisthorchis felineus (45).

Wells (46) notes that investigators of ascaris, while studying these nematodes, suffered from attacks of sneezing, lachrymation, itching and swelling of the fingers; another one from a severe attack of conjunctivitis with chemosis, after having touched his eye with a finger that had been in contact with one of these worms. The probable causes of these toxic effects are discussed by Wells in detail.

All the foregoing observations, which bear the character of experiments on a large scale, seem strongly to support the contention that what by some has been supposed to be cancer contagion appears, in reality, due to infection with non-specific agents from a common source:

Bashford also comes to the same conclusion: viz.: that cancer is not contagious, on the basis of a very thorough investigation of five of the best-known instances of reputed "cancer houses"; he declared cancer houses generally, from the viewpoint of contagion, to be myths (47). He had previously approached the "cancer house" question statistically. In cooperation with the British Bureau of Vital Statistics Bashford compiled a table (48) for the year 1905 of the number of deaths to be expected under the law of probabilities for persons above 35 years of age, when the chance for such to die from cancer was placed at 1 in 12 for men and at 1 in 8 for women. The table is as follows:
The table shows that the expectation of cancer incidence may be high for a given house, if a family and its aged retainers occupy it for a long time and that, in the natural course of events, such a residence might become a "cancer house," but that there would be no justification in using the occurrence as a proof for cancer contagion.

With that we can leave the "cancer houses," "cancer streets," and "cancer regions," which undoubtedly exist, thoroughly convinced though that the contagiousness of cancer has not been proved and, to my mind, equally convinced that it never will be proved. But that parasites may, on occasion, be actually concerned in some way in the etiology of cancer seems equally certain. On examining a specimen taken from a very small carcinoma in a mouse, Borrel saw (49) the furrow of a worm which had left the tumor, and at the end of the furrow he found the worm. One of his pupils (50) found in 8000 autopsies upon rats, 6 cases of sarcoma of the liver with cysticercus. In one of the cases five worms had given rise to five separate sarcomatous foci in the same lobe of the liver; in another case a worm was found at the center of the tumor. But that there is nothing specific about these parasites is proved for one thing by the finding of a rusty needle at the center of a carcinoma (51); proved, secondly, by the fact that cancer results only in a small percentage of the cases of parasitic infection; and proved thirdly by the fact that parasites specific of other diseases may yet be the inciting factors of cancer; e.g., the tubercle bacillus in lupus, the Treponema pallidum in luetic lesions, Trichinella spiralis in trichinosis of long standing, of which latter Fibiger (52) quotes many cases from the literature.

The strength of the contention of the non-specific character
of the parasites becomes particularly evident if a parasitic Bilharzia carcinoma of the bladder (26) is placed in parallel with an aniline carcinoma of the bladder (53). In the Bilharzia the sharp points of the eggs of the worm cause chronic inflammation of the walls of either the bladder or of the rectum in which they are lodged, and on the basis of the inflammation carcinoma develops in some of the cases. In the manufacture of aniline, laborers employed in certain steps of the process are apt to acquire catarrh of the bladder from contact with the chemicals. If these laborers are promptly put to other work upon the onset of the catarrh, the symptoms usually recede; but if these patients continue to remain exposed to the deleterious chemicals, the catarrhal inflammation of the bladder becomes chronic and in a certain percentage of the cases turns into cancer. Cause and effect are here established with the exactness of an experiment. Cancer arises from purely chemical influences, no cancer developing when the chemical influences are eliminated at the proper time. It would seem that in both cases a chronic inflammation was the point of origin of the cancerous development and that it is irrelevant what cause maintains the chronic inflammation, be that cause alive or dead, organic or inorganic.

Such observations rather shake the foundations of the contagium vivum and its specificity. No analogy exists between cancer and any known form of infectious or contagious disease (54). The possibility of the transference of cancer cells from one individual to another is non-existent (55). In cancer à deux, so-called, if the husband has cancer of the stomach and the wife cancer of the uterus, and the theory of contagion were correct, then either cancer should be a metastasis of the other, and the husband should have a cancer of the uterus in the stomach, or the wife a cancer of the stomach in the uterus. No such case is recorded in the literature (56). Cancer appears in every instance as an individual experience, unrelated to that of other individuals (55). Parasites, when entering into the etiology of cancer, appear as only one of many types of inciting factors: mechanical, thermal, actinic, chemical, endocrine, hereditary (57), all of them equally potent and equally impo-
tent, in that their presence may or may not induce the onset of developments tending in the direction of cancer. They are the match that lights the fire, and their relation to cancer appears as distant as the heat of the fire is from the flame of the match (57a). They incite, but are merely incidental.

At this point we will leave the consideration of parasites entering the human system from without and turn to another aspect of the parasitic theory. We have to go back as far as Johannes Müller, the first man to examine a cancer under the microscope, whose still famous handbook on physiology appeared in 1835. Müller conceived the idea that the cancer cell as such had all the characteristics of a parasite (Orth). His suggestion was lost sight of and, it seems, was completely forgotten in the strenuous efforts to discover the *contagium vivum* or specific agent of cancer. But it had a re-awakening. Toward the end of the last century a number of investigators considered the cancer cell itself as an immigrant parasite (58). But when it was proved beyond contradiction that cancer cells descended from pre-existing tissue cells, the ground was slightly shifted and the contention was then brought forward that cancer cells were not real parasites but merely acted like parasites, and with that Johannes Müller came again into his own. This view acquired a most distinguished following: Hauser (59), Orth (60) Ribbert (61), Borst (62), Abderhalden (63), and many others of equal prominence.

The contention is based on the observations:

1. That cancer cells form no tissue, but ordinarily lie disconnectedly and loosely side by side in the stroma (64), and without physical connection with the stroma, so that they can be shaken out from thin sections (65).

2. That cancer cells perform no function in the system, nevertheless live upon it, and when appearing to function—as in the well-known case of v. Eiselsberg (66) in which, after extirpation of a cancerous thyroid gland, the typical myxoedema was overcome by a metastasis which took up the function of the gland—such functioning will last only a short time and then cease (67).
3. That cancer cells acquire so large a measure of independence from any particular tissue that they can be disseminated throughout the system like bacteria, and when so disseminated, seem to act like parasites (68), in that they form metastases wherever they find lodgement, and that such metastases are structurally like the primary growth.

4. That cancer cells, like a microbial infection, are capable of producing thrombi in veins (69).

Seemingly the conception of the similarity of the cancer cell to a parasite was, in its turn, badly shaken when experiments succeeded in which cancer was propagated by means of cell-free filtrates of cancer tissue and also by means of the dry powder of cancer tissue (70). Here the structurally intact cancer cell, the alpha and omega of the adherents of the cellular theory, had been totally eliminated. The question of the etiology of these neoplasms, as revealed in their experimental propagation, was by such elimination apparently reduced to a choice between a chemical virus and that last refuge of the adherents of the specific parasite—the invisible contagium vivum, a protozoon so small as to escape ultramicroscopic detection.

This last assumption tended to bring the specific parasite of cancer again to the front. If it were to be driven from this last lair, it would then seem to have been reduced to a dead issue.

In this connection it must first be conceded that there are quite a number of infectious diseases, e.g., Texas fever, hog cholera, goose pest, variola, trachoma, lyssa and possibly measles and scarlatina, with infecting agents so small that these agents pass bacterial filters and are beyond the reach of the ultra-microscope (71); their place is apparently between bacteria and protozoa. They, or at least some of them, are harmless to one set of warm-blooded animals and harmful to another. Thus, e.g., was the sleeping sickness of South African cattle traced to nearby herds of germ-carrying antelopes which themselves were in perfect health, while the cattle when infected with the same germ died. The antelopes were killed off, and after that there was no more trouble with the cattle. The
tsetse flies kept on stinging the cattle but, being no longer infec
ted from previous feeding on antelopes and, therefore, acting
no longer as intermediate hosts of the infecting agent, their
sting had become harmless (71a). Research in these matters is a
science in itself, and their further discussion would be going
rather far afield. But what is here worthy of note is that the
invisible parasites of the diseases mentioned are specific and,
where harmful, always produce the identical and readily recogn-
izable symptoms (71); secondly, that the diseases which they
induce, if the patient survives, are always limited in time (72).

That is quite different from cancer conditions. Tumor growth
is always unlimited in time. The tumor may have its periods of
retarded progress, even periods of recession (73), but, if left to
itself, there is no termination to its growth except by the death
of the carrier. Spontaneous healing, which would be a limita-
tion in time, is a rare occurrence and seemingly always due to
extraneous circumstances having no direct connection with the
cause of the tumor growth (74). Again, as to identity of symp-
toms, there never are two tumors perfectly alike; each tumor is
a law unto itself (75). Again, "the observation made regarding
neoplastic growths," says v. Hansemann, "viz, that the same
etiological factor causes the growth of different tumors and, on
the other hand, that similar tumors owe their origin to different
etiological factors, is quite incompatible with bacterial infec-
tion" (76). Clearly, then, the alleged invisible specific cancer
agent can have nothing in common with the aforesaid invisible
specific infecting agents save its ultra-microscopic size. Orth
considers a sarcoma produced without intact cancer cells not a
transplant, not a secondary, but a primary tumor (77). As
regards the etiology of these new growths resulting from filtrates
and powders of cancer tissue, the chemical alternative to the
invisible specific parasite would consequently appear the more
promising to pursue.

Aside from all the improbabilities advanced in the foregoing,
as to the existence of a specific cancer agent, and aside from
many other related improbabilities, such as the necessary
synchronizing of cell division and parasitic division in order to
provide each new cell with an infecting agent (78), there re-
mains still one argument against specificity, an argument of
such importance that it should once more be emphasized. The
most enthusiastic supporters of the parasitic theory of cancer
admit that the formation of benign tumors cannot be due to a
parasite (79). But a clearly defined borderline between benign
and malignant tumors exists neither in theory nor in practice
(80), and this is proved anew by the increasing number of cases
in which non-specific parasites are shown to have been the in-
citing factor in the formation of benign as well as malignant
tumor growths (81). And now we come to the point to be
emphasized: viz, that inasmuch as "no sharp line can be drawn
between benign and malignant tumor growths, a theory is wrong
in principle which covers only carcinoma" (Herxheimer (82)).
"A theory or hypothesis designed to fit only cancer starts
wrong, and is of no value for the much broader problem"
(Borst (83)). "No theory of the causation of tumor growth can
be satisfactory which does not apply equally to innocent and to
malignant tumors" (Catheart (84)). "The adequate theory
of neoplasia must be one which will explain not cancer alone,
but all types of tumor formation. No parasitic theory suffices
to do this" (Adami (85)).

After half a century of searching in many directions science
has returned to the starting point. Virchow's theory that
irritation is the cause of cancer—and after all, the effect of a
parasite within the system is also but an irritation (86)—the
conception that the soil must first be prepared by disease before
developments tending in the direction of cancer can take place
(87), remains the dominating thought.

"The era of the parasitic theory, working with morphologically
describable tumor agents, is behind us. Whenever parasites are
now brought into genetic relation to tumors, their influence is
looked upon as merely indirect. Not parasite plus cell reaction
induces tumor growth, but parasite plus tissue reaction induces
inflammatory hypertrophic processes which, in a certain number
of the cases, are followed by tumor formation. Not infection,
but irritation is the underlying factor" (88).
Irefutable proof of the correctness of these latter conceptions has been rendered, as stated in the beginning of this paper, in the experimental production of primary carcinoma by means of irritation. That procedure is now an actual reality and is being practised in research laboratories as a matter of everyday routine.

A new era of cancer research has thereby been inaugurated and is evidently bringing us measurably nearer to the solution of the cancer problem.

**SUMMARY**

1. By general agreement of competent investigators the observation is throughout accepted as a fact that spontaneous cancer cells descend from normal cells of the tissue in which the cancer arises.

2. To the process of transformation of the cells from one state to the other, parasites, like numerous other non-specific factors, such as mechanical, thermal, actinic, chemical, endocrine, hereditary, stand in the relation of the match to the heat radiating from the fire which it has kindled, viz, inciting but incidental.

3. Current experimental production of primary cancer by various non-specific means makes the search for the specific cancer agent appear as no longer advised, and seems to prove that irritation is ordinarily the starting point of developments tending in the direction of cancer.

4. As nearly as anything can be certain in medicine, there is no cancer contagion, i.e., specific infection.

5. Observations seem to prove that cancer is in every instance an individual experience.

6. More than one individual may receive a non-specific inciting factor from the same source, and, then, independently, by reason of the same, may or may not develop cancer.

7. Around a source disseminating directly, or indirectly through intermediate hosts, one or more non-specific inciting factors, "cancer houses," "cancer towns," "cancer districts" may grow up.

8. In order to reduce cancer incidence such common sources
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should be sought out and abated. One such source seems to be the rat.

9. Systematic rat extermination, already suggested (89) for economic and hygienic reasons, appears advisable also from the point of view of reducing the number or cancer-inciting factors.

10. From the same point of view prophylactic anthelmintic treatment at frequent regular intervals throughout life, applied as broadly as vaccination against smallpox, might possibly work a reduction of cancer incidence. Such a proceeding would, of course, be of still greater value if in addition means could be found to reach and render harmless the larvae in the various organs.

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