CHAPTER III

THE PATHOGENIC MECHANISM

When one compares the tireless activity of the child with the aches and restriction on motion as age advances, it is evident that the exchanges between the tissue parenchyma and blood stream of the child have no impediment so that waste products get out as fast as formed, and oxygen fuel and food enter as freely as is required for full combustion and tissue construction. There is no separating fibrosis between the parenchyma and the blood supply. In old age the separation reaches the limit where the exchanges are practically abolished, and finally, where life is no longer supported. One organ or other as habits and heredity have determined has suffered most at the hands of the fibrogenic agent, and cerebral paralysis or heart or kidney failure may be the immediate cause of death.

We have identified the initiating factor as an activated amine which causes a gellation of the plasma and cellular colloids and this gellation blocks the transport of oxygen causing a local hypoxia or anoxia. In addition to producing the gellation as we have observed results from the guanidin poisoning in our parathyroidectomy work, the amine condenses firmly with the tissue function carbonyl groups so as to block its initiation of energy producing oxidation chains. Incompletely burned metabolites of tissue cell origin or of germs caught in the anoxic area, then may be dehydrogenated so as to become free radicals but under the anoxic state cannot be burned. Since the amount of dehydrogenation accomplished under such circumstances is small at any time, a slow polymerization of the metabolite can proceed. This is especially true where scarring has reduced the oxygen transportation. The free radicals, be they of tissue cell or germ origin, may copolymerize with each other too, or with the collagenous material that is produced by fibroblasts in response to the irritant effects of the incompletely combusted state. Thus they are incorporated into the fibroblastic tissue intended to dis-

pose of the toxicity. Cancer cells likewise we hold, take up the toxic products into their structure in the same way and thus serve as detoxication agents. (Koch, Cancer and Its Allied Disease, 1926, Koch, Cancer Journal, October, 1924.) As the fibers increase by added deposition of collagenous and toxin co-polymeres the last depositions made present the highest molecular weight, and as each such group produces a characteristic set of disease symptoms, each fiber carries a history of the intoxication from the inception of the anoxia. The same appears to be the case for each cancer cell as well. If the cancer cell could complete the combustion of the toxin, it would offer protection and serve the immunity mechanism, which we feel is its intended goal (Koch—Cancer Journal, October, 1924) in antitoxic hormone evolution.

SYMPTOMATOLOGY OF CANCER

The Pregrowth Phase

The constitutional nature of cancer was well demonstrated by Glover in 1926, when he showed that the pleomorphic organism that was responsible for the disease could be isolated from the blood long before a growth made its appearance. He published in the Canadian Lancet and Practitioner of that year. He also demonstrated the germ in all cancer tissues that were examined, and proved the etiological position of this germ in fulfillment of the four laws of Robert Koch. Of course he further proved his point by developing a curative serum, and that brought the wrath of the profiteers on human suffering down on him. His persecutions are too distasteful to mention here, and too disgraceful to Canadian Medical and American Medical Association leaders to think of. At any rate his great service was lost to the world all this time, and only now at the International Congress of Microbiology held at Rome in Sept., 1953, was Glover's work presented by Dr. Geo. Clark, who with Dr. Engle, repeated the work with full success under the auspices of the United States Public Health Service. However the government did not allow them to publish their results. The exposition at Rome therefore is a great advance for truth. Contemporaneously von Brehmer discovered and developed the same facts

in Germany, using a different technique. But his announcements were not made until a few years after Glover made his. Von Brehmer has the support of the bacteriological faculty of Germany who made a critical investigation to throw it over if possible, but found that the organism was what von Brehmer claimed and what Glover found too, a pleomorphic germ showing varying morphology, bacillus, filiment (fungus), coccus and filterable virus. The cocci are spores that develop in the bacilli. Glover showed that all morphological phases give rise to the virus and bacilli. Besides many other bacteriologists have confirmed these researches in so far as their own investigations have dove-tailed with them. Both Glover and von Brehmer have confirmed the etiological position of this organism serologically by developing an antitoxic curative serum that showed gratifying efficiency. As the German commission reported, it is therefore a bacteriological entity independent of other germs serologically.

This of course means that cancer is an infectious disease, as we have always claimed also, and the existence of the infection in the system should give rise to symptoms. We made our investigations on that point from 1914 on and published our findings in the Medical Record of New York in October, 1920, and in the Cancer Journal of 1924, as well as other papers. Our observations showed that the Flu epidemics of the first world war gave cancer a boost, and the symptomatology was much more intense after this event. As a rule the pregrowth symptoms were found to exist five to twenty years before the growth came and the longer they existed in the parent with cancer, the shorter their appearance in the off-spring that developed it. Thus the pregrowth toxic period became shorter and the growth appeared earlier in life besides, by some five to ten years as a rule, in each successive generation that showed it—quite a virus characteristic.

The symptoms are generally a neuritis which may be rather violent, and exist in the arm or shoulder in cases that develop gastro-intestinal neoplasms. It may show up as a Sciatica, or a dizziness, or an epilepsy, headaches, visual disturbances, etc. The nervous tissues seem to be the favorite site for the toxic

action, but there may be a psoriasis, some skin allergy, or a compulsory neurosis, while the lymphatic reticulo-endothelial system undergoes some atrophy. Before the growth comes, for some six years or so there may be a gain in useless fat, of a watery variety and weakness develop concomitantly. After the growth comes the symptoms disappear wholly or in part, only to return again if the growth is removed, and again disappear with the recurrence of the growth. Depending upon the rate at which the toxin is produced as compared with the rate of growth of the neoplasm and its absorbing and copolymerizing with the toxin, the latter is stored out of the way more or less and the symptoms will disappear proportionately. (Koch, Cancer Journal, October, 1924. Koch Cancer and Its Allied Diseases, 1926.)

We have interpreted this affair as a protective action of the growth through which in time it may not only learn to absorb the poison and take it out of the blood stream and tissues, but also learn to destroy it. The increase in the neoplastic activity generally follows the rate of toxin production, and so we argued that if the toxin (virus) could be done away with, the growth would become obsolete and disappear. Our experience shows that this is exactly the case. We diagram the integration of virus and toxin with tissue functional structures later on.

To illustrate this situation, it can be done no better than to paraphrase a letter received last week from Pasadena, California. It runs as follows—"In 1932 I brought my mother to you from La Cross, Wisconsin, with cancer of the stomach. She was an advanced case, and the symptoms she suffered for years before the tumor was discovered are being repeated in me. I am asking your advice about an exploratory operation to see if I have what my mother had, and the doctor's examinations here indicate that I have, and only time will give the full proofs. Since your treatment was given my mother and she got well and lived fifteen years longer and died of a heart attack, I have confidence in your advice. I started out with a terrible neuritis in my left arm, and could not raise it above my head. It increased in severity until I had to carry it in a sling for months. It gradually left there and went to my sciatic nerve. I also fell and hurt my knee. Tetanus antitoxic serum was given me and I de-

veloped a terrible urticaria that nothing helped except Cortisone. Then my body became covered with boils and I am taking an antibiotic for that, but have to keep it up. Before the trouble located in my abdomen, I began to take on weight and dieting has not helped a bit. Obstructive symptoms in the abdomen are the trouble now, and the neuritis has improved a great deal. This is the way my mother's cancer developed." Such reports are the rule, with slight variations. But there are exceptions also.

The fact that the toxin causing the symptoms can add to the structure of a developing fibrosis or of developing cancer cells, shows that it presents either highly polar double bonds or free radicals as we explain later, and hence exists as a sub-oxidized residue of some sort of metabolism, tissue cell, germ or virus in the sense offered below, and operates as we diagram later. This incompletely combusted state, and the anoxia that governs it are the important factors we must consider to secure a correction.

Tissue burns from steam or fire produce similar incompletely burned products which are irritating, and the incompletely combusted products of heart muscle activity under coronary insufficiency cause the pain here too. Completion of the combustion in cases of burns, or during a coronary attack, has brought grateful relief. And it should be evident that efficient oxidations would have prevented the pathogenesis as well. The aging of tissues that goes with this toxogenic fibrosis is easy to understand, and the toxins that cause cancer must certainly add to the rate of aging by their stimulation of fibroblastic tissue. Blood plasma of patients with cancer or developing it should show this effect. Case histories that follow show how the fibrosis can be disposed of by supplying highly activated carbonyl groups. We have observed how burns stop paining and heal quickly with minimum scar formation after the catalysts are given, and how the fibrosis of the sclerotic liver, kidney, heart, and brain, disappear after many years of accumulation and hindrance to function. Case histories will demonstrate this. It is a sociological matter of the highest importance.

After the treatment is given the symptomatology of the

years of the pathogenesis is repeated in reverse order to its production. (Koch, Cancer and Allied Diseases, 1926). That is, the last set of symptoms or tissue change to come are the first to flare up and disappear, and the first to come are the last to be repeated transiently and then go for good. Such exhibitions come at cyclic periods that are multiples of three weeks, and follow a definite characteristic course which is informative as to the status of the recovery process. Thus finally after a neoplasm has been absorbed, there may be a sudden intense inflamation of an old scar from a wound, or in the tonsil on the same side as a breast from which cancer was absorbed. This may last a few days and then be gone and with it the induration of the lymphatic glands of the region as well. As the fibers of the scar or interstitial deposits undergo depolymerization as a result of the oxidation chains initiated by the treatment the more superficial deposits are liberated and depolymerized first, and so have a chance to show their symptoms as they are being degraded and burned out of the way. Thus the last symptoms to come are the first to go, and that includes the neoplasm, or the coronary fibrosis, etc. Finally, after the acute inflammation has come and gone, one may conclude that the toxic unit as first produced and incompletely burned, is now out of the way, and with it the pathogenic agent. The cure is then complete. The cyclic reactions, and the retracing of the symptoms of the pathogenesis in reverse order is an established characteristic of this treatment which distinguishes it from all allopathic affairs. The cycle phenomena indicate the basic nature of the recovery process.

Evidently fibrogenesis and neoplasia are both detoxication attempts, and where fibrogenesis becomes exhausted, or is unable to get started as in infants, neoplasia asserts itself. Thus they appear to both be imperfect complimentary processes in which fibrogenesis (mesodermic protection) staves off neoplasia. It is evident too that the dehydrogenations by our reagents, start the oxidative destruction of the pathogen right at the point of attachment to the host cell, where the very inception of the disease took place. The pathogenic significance of the fibrosis of "silent" focal infection is also evident.

THE PAIN IN CANCER

Pain in cancer may be divided into two categories. One is the natural pain, and the other, the pain produced by surgical and radiological injuries.

Natural Pain

The **Natural Pain** is due to exposure of the nerve endings to the air and its contaminants, because of the destruction of the superficial protection, as the malignant erosions progress. Pressure of the tumors produce both pain and painful reflexes through pressure and tension affecting the nerves. Then there is the chemical cause of the pain which resembles that caused by the incompletely combusted products of a burn, or caused by the incompletely combusted fuel products of hypoxia in coronary insufficiency. Thus the faulty oxidations of the neoplastic cells yield irritant products that may cause very intense pain.

The weight of laboratory opinion has decided that cancer cells are much of the same order as normal cells in the utilization of oxygen. However the clinical facts show that the capacity of tumor cells to use oxygen is vastly reduced, and their utilization of oxygen yields irritant by-products rather than carbon dioxide, and does so at a lower potential that is unable to provide energy for the building of the highly differentiated cell ultrastructure and gene material required by a surviving tissue reciprocity and coordination, or by the racial economy. The neoplastic products also belong to the grade liberated in the Krebs' cycle of oxidations, and these are irritant acids, which further reduce the tissue alkalinity to favor amino acid decarboxylations resulting in toxic amine products that interfere with oxygen utilization in the several ways described in this text. Moreover the energy that is produced by hydrolytic glycolysis, is not only able to support tumor mitosis but is yielded at the expense of more acid production which furthers the neoplasia as just described, and also by the pain these highly irritant acids cause. Study of the natural pain of cancer observed clinically may thus help to eliminate many of the laboratory uncertainties. The natural pain proves the quantitive and the qualitative deficiency in the oxidations of tumor cells.

We prove it also by supplying oxidation catalysts that repairs the deficiency. When this is done as described in our thesis, the irritant by-products are oxidized out of the way, and pain disappears completely or to a bearable extent, and in a very short time as a rule. Pain, due to nerve compression from fragments of erroded and collapsed bone is a different matter and always requires the relief from the pressure by proper splinting. Such catastrophes should be anticipated and proper splinting done to prevent them. Likewise pain of sphincter spasm and ballooning of some viscus wall through nerve inhibition, has its specific type of care, as by lavage, proper diet, and the correct homeopathic remedy.

Therapeutic Pain

Therapeutically produced pain is much worse, and more difficult to treat than the natural pain. The necessary stretching of tissues incident to radical surgery cannot be avoided. But the destruction of the blood supply favors more rapid recurrence with necrosis and infection and increased production of incompletely burned metabolites and increase in the pain in a way that soon catches up with the status had it not been operated. Ewing's summary is conclusive—pp. 597-8 of the 1942 Text on Cancer—"In estimating the economic importance of the surgical treatment of mammary cancer there must be charged up the cost of acquiring surgical skill, and the deplorable conditions following local recurrence. There can be no doubt that operation shortens life and *aggravates the terminal suffering* in the great majority of recurrent cases." (Italics are ours.)

Yet the chief cause of therapeutic pain is irradiation. Oxidation deficiency throughout the whole irradiated area is added to that naturally produced, and incompletely combusted irritant products increase with the extensiveness of the irradiation to add to the pre-existing misery. Even though mild irradiation may show no pain effects, the products of the incomplete combustion it causes, may announce their presence in other ways. This situation requires illustration to be understood. In 1941 while visiting in Rio de Janeiro, a leading internist offered a case for treatment, that had baffled all the experts far and wide. This was a young woman of high social position and a remark-

able beauty. She wished to be married, but this could not be done until a mortifying skin condition could be made to disappear. Her whole body was covered with small black pigmented spots from three to ten millimeters in diameter. They started to appear two years previously and increased in intensity steadily month after month. She carefully avoided the sun light, but it did not reduce the increase in the intensity of the pigmentation. A chain type catalysis was therefore evident, and I suspected two factors that would compliment each other in producing the condition. One is some form of irradiation as the X-rays, and another a special sensitiveness lying dormant in a suppressed tendency to pigmentation. Thus a trace of negro blood which is common in Brazil would provide the sensitivity. Inquiry also showed that she had received some X-ray therapy six months before the spots began to appear. The therapy was light, and for a very mild skin complaint that would have cleared up on diet alone. On the theory that the irradiation produced incompletely combusted products that acted like those of a burn from the sun, but in self perpetuating progression as the effects of irradiation are, I figured that completion of their oxidation would destroy their pigmentation exciting effects, and the hereditary tendency to make the response would lose its stimulus, thus the spots may disappear. The treatment was given and they were gone for the most part in seven months, and those that still remained were scarcely noticeable. The girl was married and is reported to have lived happily ever afterward.

Other effects of the suppressed oxidations may extend to the offspring and result in physical defects, or they may suppress function and cause tissue atrophy in the subject himself. In such instances the cell ultra-structure and gene material are injured so they cannot conduct their oxidations. Consequently dependent function fails. The irradiation pain is comparatively a crude effect in contrast. Likewise suppression of the "ultra-oxidations" removes the protection against leukemia, and are hindrances to endocrine development and function. The whole gamut of irradiation has now been used and the turn from the X-rays to isotopes is about the same as leaping from the frying-pan into the fire. Intra-atomic defects are produced both ways

and such defects cannot correct the inter-atomic defects that make up the various diseases. So how can they cure? Suppression of reaction to disease agencies may give symptomatic relief for a time. But the disease only gets a better chance to imbed itself and spring forth when least wanted. We hope that a frank estimate will be made of this subject some day and that when accounts are balanced, the physiological view will be considered and advanced with the same vigor as was given to irradiation therapy.

The high cost of narcotics that must be used but finally fail to quench the pain fire, and the general injury to the tissues, and especially the brain injury by the irradiation narcotic combination are to be considered too. Edema of the brain brought about in this way, with its terrible hallucinations, and the horror of distorted ideas, ravings, etc., offers about the worst way any one can pass on into eternity. Thus a religious problem is concerned. Irradiation is given to reduce pain. The first few applications have a numbing effect on the nerves so that pre-existing pain disappears, but as the nerve injury develops the numbing effect disappears and the pain returns with steadily increasing severity until opiates fail to relieve and it becomes necessary to use some form of intravenous anaesthesia, until death comes as a mercy.

THE KREB'S CYCLE

Decades ago Prof. Roger Williams taught that the injury a surviving tissue preparation suffered, would partly or totally hinder its performance of oxidation of sugar, and that the intermediaries so often isolated and credited with what was later designated the "Kreb's Cycle" are not to be found where the tissue oxidations progress unhindered. Besides this injury to the tissue, which makes it anaplastic or deficient as does anaplasia in cancer cells, the circumstances of oxygen transport and waste product elimination in the tissue slice in the respiratory chamber, set up reverse equilibria that lead to carbon dioxide fixations, that are observed to increase the number of carbon atoms in the sugar chain to more than its six when it is supposed to be broken down to shorter chains. It is not surprising that the Krebs Cycle pictures an anaplastic hypoxic metab-

olism much like the cancer cell exhibits, and that therefore, the cancer cell is not of the order of the normal in its oxidations. Instead the bit of tissue studied in the apparatus does not represent the normal at all. The error of the bio-chemist on this question is very serious, and is one of the great hindrances to the progress the conquest of cancer should have enjoyed for decades.

Waters called attention to the fact that the dehydrogenation of succinate to fumarate could not take place in an aerobic medium, since the free radical formed would add molecular oxygen and form a peroxide free radical that would start other oxidation chains than those of the Krebs' cycle or break the molecule down to shorter bits. Only in an anaerobic medium could fumarate be formed, and the Krebs' cycle is supposed to not deal with an anaerobic medium. Water's criticism is in agreement with our own, since we figured that the fumarate formed under anaerobic dehydrogenations, would lay over as a preserver of aerobic chain oxidations when oxygen again was admitted to the field or when true oxidation catalysts could be supplied. Thus the anaerobic fumarate product preserved the aerobic status of the tissues through its carbonyl groups as activated by conjugation with ethylene linkages, and therefore as dehydrogenators, that are able to initiate chain oxidations in the presence of molecular oxygen.

Tissue cells appear to be well supplied with dehydrogenases in a wide range of oxidation reduction potentials for specific action on the residues encountered under hindered conditions of sugar oxidation. They doubtless keep the field clear for the high efficiency "smokeless" process of energy production that leaves no trace of its action by way of isolatable intermediaries. We have concluded that they serve as an alternate pathway for oxidation when the master "smokeless" system is hindered by hypoxia, or integration with a virus or certain amines or carcinogens. Biochemists do not admit the existence of this master process since they cannot trap its intermediaries. But we have practical proof of both its service in metabolism and the mechanism by which it operates. These cannot be denied any more than the existence of citric acid and the di- and tricarboxylic

acid oxidases so neatly assembled in the Krebs scheme, which we hold to be a secondary pathway still available to such hindered cells as cancer cells.

Oxidations on the Krebs cycle level offer no protection against virus or neoplastic parasitisms, but instead are necessary for their support. The Natural Immunity, universally observed, requires a higher order of dehydrogenation to start oxidation chains in the pathogens of neoplasia and virus diseases, and when this is hindered so as to permit disease, it can be restored by use of catalytic doses of highly activated carbonyl and free radical dehydrogenators that operate at much higher potentials than those of the Krebs cycle. The existence and nature of the **Master Smokeless System** is thus identified.

The dehydrogenases of the Krebs cycle operate under physiological conditions (pH 7 and 30° C.) with E_0' at from + 0.38 to —0.293 volts, and at normal electrode potentials (pH 0 and 25° C.) with E_0 at from 0 volts to + 0.464 volts. Moreover the reversible succinate-fumarate system is calculated at + 0.437 volts at pH 0, and 25°C., but is found by use of indicators in bacterial systems to equal + 0.005 volts. The normal potential of the lactic acid-pyruvic acid system is placed at E_0 equals —0.2 volts while the E_0' equals —0.18 volts at pH 7, and the E_0 of ascorbic acid is placed at + 0.390 volts while the E_0' value is stated to be + 0.058 volts. These may be compared with the E_0 of benzoquinone-hydroquinone which is placed at + 0.699 volts, parabenzoquinone being 0.715 volts, as usually stated.

One would look for oxidation-reduction potentials of a higher range than those that operate during the Krebs cycle to burn adrenaline or DOPA during function, with their E_0 at + 0.80, and E_0' at + 0.38 volts. Other toxic amines and pathogenic viruses call for much higher oxidation potentials, the lowest of which serves fairly well at E_0 + 0.715, while others operate at much higher levels. Since these can be used to substitute for the Master Smokeless system dehydrogenators when the latter have been inhibited from action, we conclude that the main course of the oxidations may provide for oxidation-reduction potentials much higher than those involved in the Krebs cycle. At this high potential not only a greater range of fuel, but also toxins

and virus can be burned, and the system of energy production that supports life also protects itself against injury. However when hypoxia supervenes or anoxia exists this protection may be soon exhausted.

In comparison to this system the Krebs cycle holds second place and is set in motion when lactic acid oxidase converts the product of hydrolytic glycolysis into pyruvic acid, under conditions that suspend the Pasteur Effect, we conclude, and these conditions are anoxia, virus and neoplastic parasitism, and various toxic amines, as a rule. But anaplasia or destruction of the particulate cell structure by manipulation can also annul the Pasteur Effect, proportionately.

From what has been stated here one must not conclude that the therapy is simply the use of the highest possible oxidation-reduction agent. No, indeed, each disease picture has its appropriate dehydrogenator that fits somewhat as a master key fits a lock. The disease picture, however, has variations so as to present a class of syndromes that overlap with other classes. The degrees of activity of a given reagent therefore vary within each class and among the several classes that apply. Steric hindrance is determinative here as is explained farther along.

When we consider that the neoplasm or the interstitial fibrosis started out as a repair process to correct a chemical or a mechanical injury in the presence of a toxic factor under varying degrees of hypoxia or anoxia, and the new cells attempting to accomplish the repair built into themselves the toxic elements, they could not burn, as a copolymerization process, each clinical picture presents its bound toxin in a variety of forms and in a variety of ways. Therefore the dehydrogenator in addition to possessing the correct potential of action, must certainly possess other qualities that permit it to fit the toxin molecule it is to attack in its variety of combination. For example, benzoquinone has established its value in the treatment of a variety of diseases including certain cases of cancer. In some cases its action approached the miraculous, in others it scarcely showed any effect and had to be replaced by the serial system of carbonyl groups, with free radical terminals.

The various molecular structures presented in Plate III (page 88) show different arrangements of the carbonyl group, and others as diquinone and ortho-quinone might be added. The latter offer no advantages that we have seen so far. Yet a larger experience might show such an advantage. In all, the electron contributions from ethylene and carbonyl linkages to a certain carbonyl group are different, as are their molecular weights and spacial arrangements which inspection will show. One should also consider that even the same substance in different states will show activity variation of maximum or zero value. Thus Maleic anhydride, in which all double bonds are coplanar can enter polymerization reactions readily while the esters or the plain acid is non-reactive. The same holds for its curative action in certain forms of glandular tuberculosis that we have ourselves observed. In the esters and acid only one carbonyl group is coplanar with the ethylene linkage at the same time, showing steric hindrance to meet a perpendicularly attacking radical. Even at this time our selections of active molecules in various conditions is still crude and requires much more classification of the clinical data at hand. More will be stated on this subject in the completed text. Here we see that we have a choice between carbonyl activated in various ways by electronic migrations from ethylene groups in different degrees, and from other carbonyl groups in different set-ups, and also of free radicals terminal to carbonyl group chains. Then there is the peroxide free radical we have finally succeeded in producing safely and effectively for clinical use. It is stable in solution only a few hours, but in this time it was able to initiate curative oxidation chains in the tissues that none of the other molecules have yet succeeded in producing, and our stride toward the best cure rate in neoplasia has been advanced greatly and it is more effective in other virus diseases also.

Since the natural protection can be duplicated and even greatly augmented by free radicals and peroxide free radicals of appropriate structure, we are convinced that the master oxidation process is not only initiated by carbonyl groups of high potential, but is carried by free radicals and peroxide free radicals as a chain process. Such facts place the tissue oxidations in

an entirely different light from that of current notions, and show that the free radical and the chain process it initiates is a real feature of the most efficient grade of metabolism.

PARASITE HOST CELL INTEGRATIONS

Diagramatic Presentations

We have long looked upon the **integration of virus and host cell to be an azomethine condensation between the virus amine group of highest activation, and the host cell carbonyl group of highest activation, the group that starts the oxidation chains in fuel and toxin substrates by dehydrogenation.** Let oxygen lack intervene and the virus is no longer attackable by an oxidation chain started at a carbon atom alpha to a double bond. It is free to form a condensation with the host cell carbonyl group and draw energy from the host at this point, since inactivation of oxidation initiation destroys the Pasteur effect and lets the hydrolytic glycolysis system in to produce energy in uncontrolled fashion. Thus the virus can shunt off the energy from the host cell. **Moreover the free radical formed in the virus during hypoxia, by the host cell's last act of dehydrogenation preceding complete anoxia, is able to attach to one pole of a double bond, let loose when the hydrolytic glycolysis system steps in,** for at this time the virus cannot condense with a host carbonyl group as it is not freed of the hydrogen atom it removed from the virus. **Thus two types of union can take place, one in which hypoxia is not essential but is favorable and one where it is essential.** These are shown in diagrams II and III. To the degree that oxygen gains entrance to the host cell, and under the conditions stated, the Krebs cycle can come to the rescue of the hydrolytic glycolysis system to aid energy production, but it cannot serve function under these conditions either, and so boosts virus synthesis and the neoplastic multiplication.

Abbreviations, F. M. — functional mechanism, E. M. — energy producing mechanism, M. M. — mitotic mechanism, H. G. S. — hydrolytic glycolysis system, P. P. — phosphate energy storage system.

(A)

Showing Functional Mechanism Incompacitation Illustrated by Diagram I

In (a) the energy passes into the F. M. normally. But after the Functional Mechanism is worn out from over work and can

DIAGRAM I

(a)

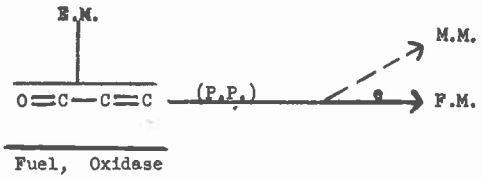
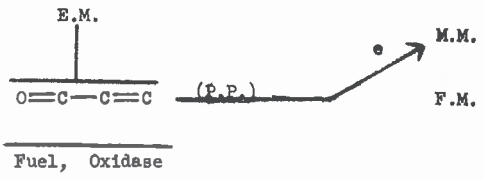


DIAGRAM I

(b)



not accept the energy, as in (b) it passes on to the mitotic, or cell division Mechanism which accepts it into its chemical processes of cell division and daughter cell construction, causing cell multiplication, with adequate functional structural provision.

(B)

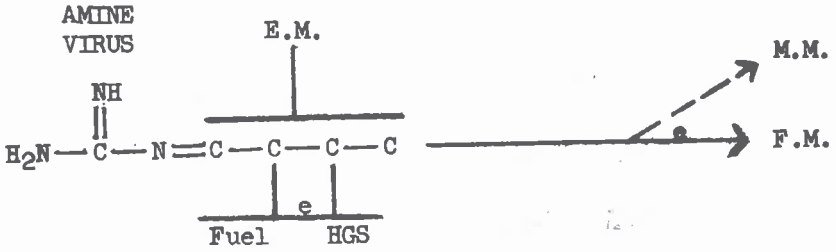
Effect of Condensation of M.F. Carbonyl Group with Guanidin, or Virus

Illustrated by Diagram II

Here the hydrolytic glycolysis system is to be remembered as acidic in nature. And the basic nature of the double bond that activates the carbonyl group that is now condensed with an amidine may be assumed to call for the association of the two. Thus the means of pouring energy from hydrolytic glycolysis into the functional mechanism is provided for even though the atomic groups individually concerned are not to be differentiated. But where a good supply of oxidase is at hand the carbonyl group will dehydrogenate and form free radicals in fuel and HGS so they can join up with the ethylenic linkage, as pictured above. This diagram also pictures the integration of virus via its amine group with the energy mechanism carbonyl group, to cause neoplasia. Blocking host cell oxidation throws the hydrolytic glycolysis system into perpetual action, supplying energy for neoplasia and for the attached virus. And the Krebs system aids with whatever oxygen is available.

DIAGRAM II

Energy Mechanism



(C)

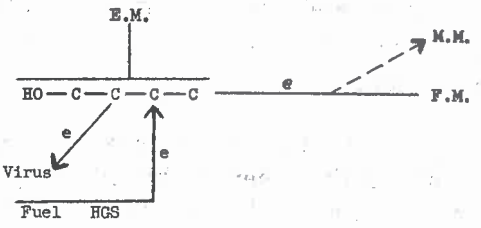
Hypoxia From Over Exertion
Illustrated by Diagram III

Here the lack of oxygen prevents the free radicals last

formed by dehydrogenation from adding molecular oxygen so they add to the double bonds of the ethylenic group. The car-

DIAGRAM III

Energy Mechanism



bonyl group is not stripped of its accepted hydrogen atom either after the oxidase serving the purpose is worn out by oxygen lack. Hence the virus amine group cannot condense with the host carbonyl group, but as the hydrolytic glycolysis system is shunted in at a double bond of the host energy producing mechanism, the pole liberated here as a free radical can condense with the free radical formed in the virus, and the energy can pass from the glycolysis system to the parasite by their close proximity of attachment. If there were no virus attachment at the pole of the double bond, of which the other holds the hydrolytic glycolysis system, admission of oxygen to the field would restore the carbonyl group and free the hydrolytic glycolysis system. But where the two poles of this double bond are taken, the bond no longer activates the carbonyl group, and it makes little difference if it is freed of its accepted hydrogen atom or not. However, if a highly active carbonyl reagent is admitted to burn off the virus, complete restoration is again possible in the presence of oxygen.

(D)

The Hook-up In Neoplastic Disease

Illustrated by Diagram IV

During good oxygen supply and carbonyl function, chemi-

cal carcinogens or virus are dehydrogenated and peroxidized and burned out of the way by a chain process. But where the carbonyl group is inactivated by condensation with an amine and cannot dehydrogenate further, and anoxia prevents the last dehydrogenated virus or fuel substrate from forming peroxide free radicals, the virus free radical will join one pole of the ethylenic double bond and the HGS will join the other by its double bond and the free radical left at the other pole in the HGS will join fuel substrate.

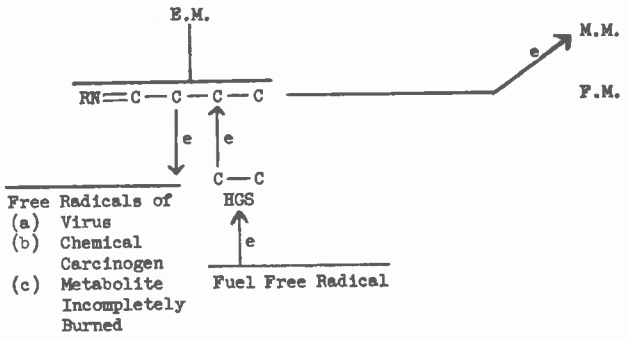
Thus energy is passed to the virus on one hand and to the mitotic mechanism on the other, each having equal opportunity to receive energy. The amount of oxidase at hand does not influence the procedure after the azomethine bond is formed, but before the functional carbonyl group is inactivated in this way the amount of oxidase will determine the number of free radicals formed in any carcinogen or fuel molecules.

The FM is destroyed or inactivated with its gene pattern by the initiating carcinogen that causes the anaplasia so all energy goes into the mitotic mechanism and the virus, and cell division does not produce new functional mechanism in the absence of functioning genes on which such a mechanism is built and patterned. Anoxia will serve much like the toxic amine since the oxidase will not be able to dehydrogenate the FM Carbonyl group much longer than when oxygen is absent. However here return of oxygen supply can accomplish a freeing of the carbonyl group and of the HGS with it.

Inspection of the diagrams given here will show why fatigue should predispose toward virus infection, and why exhaustion can prepare the way for cancer. They show too why infectious filtrates are not readily obtained from carcinomata, and why the mitotic showers occur in cycles, when one considers the hypothesis of the sprouting spore as an origin for "virus," —or maybe pseudo-virus. They indicate why dietary and hygienic measures may aid both in the prevention and in the cure of cancer.

DIAGRAM IV

(a)

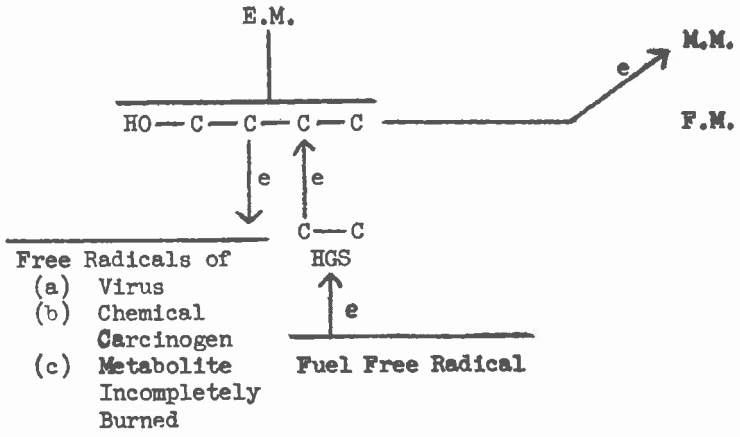


The F.M. does not exist here because of anaplasia, { embryonic / toxic / traumatic }

In set-up (a) the functional carbonyl group is inactivated

DIAGRAM IV

(b)



by condensation with an amidine of the virus, or some tight bond inseparable under ordinary conditions.

In set-up (b) the functional carbonyl group is inactivated by anoxia because of which the oxidase cannot remove the hydrogen atom it extracted from carcinogen, virus fuel or metabolite. The number of free radicals formed in this last process will depend upon the amount of oxidase that was present after the anoxia prevented peroxidations of the free radicals formed.

(E)

Lytic Virus Parasitism

Illustrated by Diagram V (a)

Here anoxia prevents the virus that was dehydrogenated from forming a peroxide free radical, so the bare free radical adds to the ethylenic linkage beta to the carbonyl group where it receives the energy formed by the HGS which has joined the other pole of the ethylenic group by a double bond. The free radical thus formed in the HGS joins the fuel substrate. The host functional and mitotic mechanisms thus are cut off from the energy yielded through hydrolytic glycolysis; and it passes into the virus.

DIAGRAM V

(a)

M.M. Inactive in Nerve Cell

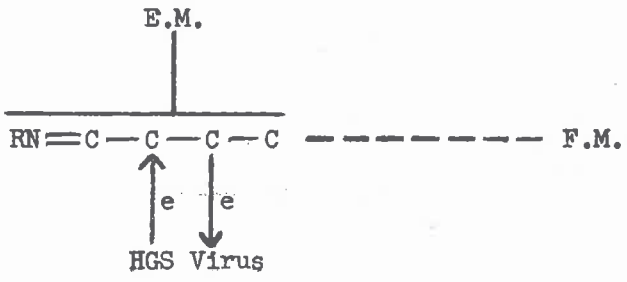
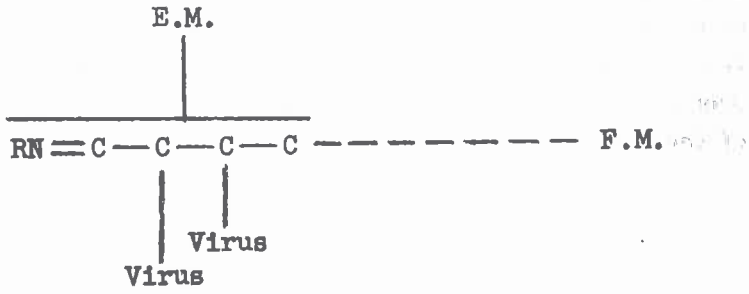


DIAGRAM V

(b)

M.M. Inactive in Nerve Cell



Supportive energy not produced

(F)

Symbiotic Virus Parasitism

Illustrated by Diagram V (b)

Here two dehydrogenated virus units join the two poles of the ethylenic linkage. Thus no HGS or fuel is hooked up with the energy production system and no energy is supplied for the vital processes except as it leaks in through fluorescent transfer from some system as the Krebs cycle which is only sufficient to keep the host and virus alive, but in a nearly moribund state of atrophy where neither can carry on any vital process of function. The Functional Carbonyl group is inactivated by amidine condensation (or oxidase failure), the amidine belonging to the virus, or some toxin (R).

This may be the state of affairs in the anaplasias illustrated by undescended testes, thyroid hypoplasia, etc. A virus or tissue or bacterial metabolic unit not fully oxidized and polymerized under anoxic conditions may offer the free radical that joins up to both poles of the activating ethylenic double bond. The amine group that inactivates the host carbonyl group may belong to the virus and need not be supplied by other toxic agents. It could be the only point of attachment of the virus which would inactivate oxidation initiation and give a path for energy from hydrolytic glycolysis to the virus and away from the vital processes of the host cell.

(G)

Carbonyl-Amine Functional Relation

Illustrated by Diagram VI

As we explained for the carbonyl-creatin interaction of the normal voluntary muscle set-up, here we picture the ketosteroid special amine relations.

Fundamental relations of this type should not escape notice for too long, since a rational explanation of function as based upon chemical structure demands scrutiny along this line in the whole realm of biology.

DIAGRAM VI

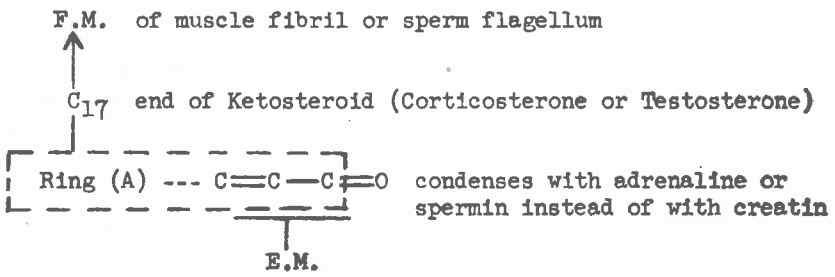
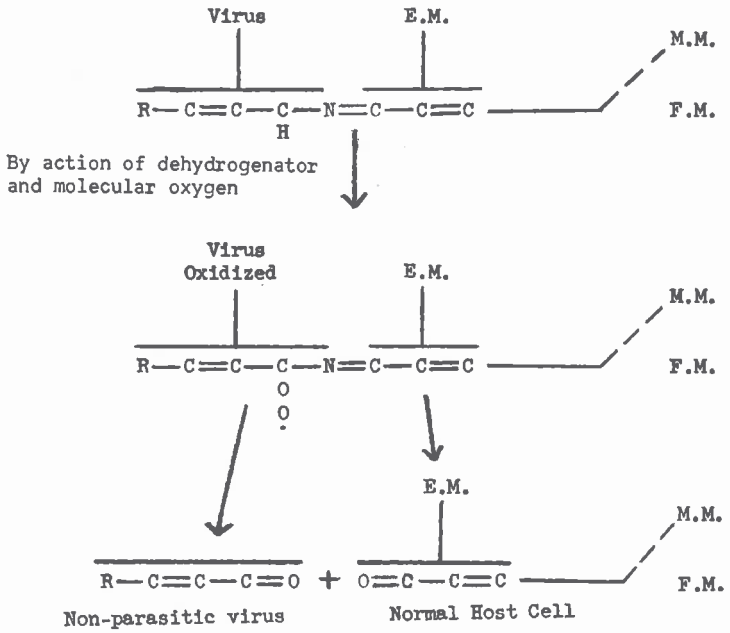


DIAGRAM VII



(H)

Oxidative Rupture of the Symbiosis with Cure

Illustrated by Diagram VII

When the virus is attached to the energy producing mechanism through condensation of its amine with the functional carbonyl group, the azomethine double bond activates the hydrogen attached to the carbon atom alpha thereto, and dehydrogenation by the remedy carbonyl group places the free radical there. Oxidation produces the peroxide free radical that splits the virus off without an amine group, but rather a carbonyl group terminal. This carbonyl group we assume is activated by a double bond in conjugation and then can conduct oxidation chains itself and no longer need be parasitic. Indeed the loss of its critical amine group excludes this possibility.

The host energy producing mechanism is left with a nitroxide free radical type condensate through a double bond which readily hydrolyses off, leaving the host cell in normal condition.

(I)

Mechanism of Fatal Vaccine Production and its Avoidance

Since the virus amine group is its means of inactivating the host cell protective functional carbonyl group, virus collected from living tissue cells may separate off with the amine group condensed with a carbonyl group from which it is readily hydrolyzable. Then when it is exposed to formaldehyde to be **"killed"** the amine group is protected from the aldehyde. Then when it is injected into a patient the protective azomethine bond may readily be split setting the active virus free. To avoid such a disaster the virus on collection should be exposed to a lower pH reaction which will accomplish the freeing of the amine group from protective condensation, and the carbonyl compound should be removed, before the formaldehyde is administered at a higher pH to assist the formaldehyde amine condensation that inactivates the virus. No diagram is required to illustrate this event. Phenol red, used as indicator to show presence of living virus, changes color at pH 7.3, and hence is cause of error as explained here. An indicator that changes at pH 3 is needed, with the medium so acidified to make sure virus amine groups are free.

Besides the conventionally recognized lytic and symbiotic types of virus-host cell integrations, clinical observations show a third type that produces no specific functional symptoms, but only shows hindrance to the tissue oxidations, weakness and the putting on of fat during the integration phase, and congestive symptoms with some fever during the oxidation of the virus off from the host cell during the cure process. This may be the type of integration that dominates during the grippe and characterizes the pre-growth phase of cancer as well as the type of union held by vaccines that block integrations of host cells with the virulent phases of the same viruses. Indeed the preparation of the host cell for the action of some chemical or metabolite of

germ or tissue cell origin that activates the neoplastic process may just be this type III form of virus integration. The "flu" epidemics of the world wars after which cancer incidence took such big strides is rather suggestive of such a situation.

It seems to us that this type of integration yields no functional symptoms as the virus concerned has no functional chemical process that can accept energy from the host cell. For to accept the energy, it must have some place to go, as for example some chemical process it can enter and activate, and which draws energy off from some specific chemical process of the host cell. It seems to us that symptoms of disease are produced when energy is thus withdrawn, or when it is passed back to the host cell, when the virus is being burned off. This holds true also for carcinogens or other toxins integrated with host cells, and so during the recovery process when the host cell is being freed of its pathogen, the symptoms that were produced during the pathogenesis are again being repeated in reverse order. Thus too, the dissolution of fibrotic tissue that walled off infection yields symptoms of the toxin as it is being broken down, and in reverse order to those of its polymerization during the pathogenesis.

The bridge over which this energy passes is the non-specific azomethine bond, or the free radical-double bond addition we have described for the integration with the host cell of virus or toxin. We also held that this bridge for energy passage that is so important to virus vegetation, and so fatal to the host cell, also provided for the cure, as it offers the double bond, or is adjacent to one which activates the alpha placed hydrogen atom, and thus serves the dehydrogenation that initiates the cure process. It is not specific for anything as any energy can pass that has somewhere to go. When the type III integrated virus is undergoing oxidative disintegration or separation, the energy yielded is not of the quality the host cell can accept into any of its chemical systems so it does not produce any symptoms of a specific function but goes off as heat and causes fever. It is also characteristic that when this fever is high, the patient feels the best ever, eats better and is much stronger. It is a different fever than that coming from the dissolution of host tissue during the pathogenesis. Many patients describe this event

with wonder during the reactions of the recovery from cancer.

One question is to be answered relating to this type III integration, where the parasite cannot use the specific energies yielded by the host cell. Does it pass this energy on from the functional mechanism with which it is ligated, to the mitotic mechanism in some such way as we diagrammed earlier? Thus if the virus were condensed with the mitotic mechanism via a free radical-double bond addition, and to the energy producing mechanism of the cell functional mechanism by an azomethine double bond, weak energy production would be assured and the path for its entrance into the processes of cell division could be visualized. The cases of cancer that recover without repetition of symptoms of specific functional interference may be explained by this assumption provisionally at least, especially when the oxidation processes are still hindered.

One has to think of the specific protein of the virus which when integrated with the host cell confers its specific serology thereto. It may be the pattern of this specific protein that accommodates the adherence of the virus to the host cell at the first collision. One sees such an event when boiling cream for its preservation, the protein material tends to accumulate after standing and cooling, as a ball, which increases to a certain point with time. Here molecules of a definite pattern fit and hang on to each other as they make contact. Vaccines may thus also work via their occupancy of the receptor spots of the host cell, and thus exclude the attachment of virulant virus covered with the same type of protein. Besides a specific digestive ability of the host serum for such protein will remove its mechanism of attachment to the host cell surface. Thus the bridge mechanism for true integration, that provides for the parasitism and its energy transfers, is not able to find entrance and gain hold in the host cell, and the specific protein antibody immunity is reasonable protection to a certain point. Thus all immunity known today must be established before the challenging infection is given. The host cell must be protected from penetration by the parasite. The cure process however, in line with our thesis and actual practice, can take place via the oxidations induced any time after the integration has happened, so long as the host cell is not injured

too badly to survive after the parasite is oxidized off. This system then is the only means of protection and cure after the virus has penetrated.

SUMMARY ON CARCINOGENESIS

It will be seen from the foregoing explanations, that carcinogenesis resides not only in a specific quality of the K region of the carcinogen that makes it liable to free radical production but also in an extrinsic event in the field, anoxia, which leaves this free radical free to join a pole of a double bond of the energy producing mechanism associated with mitosis, instead of forming a peroxide free radical and either undergoing fragmentation, or serving as the carrier of an oxidation chain that disposes of many more molecules of the carcinogen. This free radical mechanism is supported by a number of facts as for example, the interference with polymerizations shown by minute traces of carcinogens, and also the marked inhibition of carcinogenesis by azo-dyes, produced by traces of methyl-cholanthrene, while substituted amine types mutually accelerate their activities. (E. M. carbonyl inactivation).

In addition the carcinogenic act is one that causes a pouring of energy into the mitotic mechanism of the host cell, as we have tried to explain, and the electronic density of the K region is not sufficient to account for that. If the energy is transferred via fluorescence as we proposed decades ago, the electronic picture of the molecule as a whole is concerned, for the energy handed over through fluorescence from hydrolytic glycolysis (Koch, Natural Immunity, 1935), to the reactions of mitosis must be of the quality mitotic processes can accept specifically. This thesis must not be confused with the chemiluminescent theory of Anderson (1947) which as we understand him, claims that the energy liberated by oxidation of the carcinogen changed the cell protein from the benign to the malignant type as do the X-Rays. However experimental scrutiny would show that when the carcinogen is oxidized it is no longer active as a carcinogen, and X-rays break the atom down within, with a much greater energy yield than the inter-atomic action of visible and ultra-violet wave lengths that act on physiological and pathological levels. Our old theory was one of photo-sensitization in

which small amounts of carcinogen could mediate a continuous energy transfer without exhaustion.

Another matter to consider is that when the carcinogen free radical adds to one pole of the most reactive double bond of the host cell, it becomes a "substituent" with a rich conjugated system of double bonds, benzene rings, etc., which must alter very greatly the electronic configuration of the vital molecule of the host cell. In consequence to this distortion, energy production and distribution would necessarily be muddled up too, so that instead of going on to the processes of some useful function, it might be diverted to the mitotic reactions.

We are held to an explanation of carcinogenesis which will also clarify the chemistry of virus parasitism, since a broad front of carcinogenesis like a broad front of virus infection is corrected by a single reagent—the activated carbonyl group, or its trailers, the free radical in the presence of oxygen or the peroxide free radical. Hypoxia prepares the way. The clinical cure of cancer or virus infections must take the latter into consideration, as well as the "functional" hypoxia by which one may characterize the paucity in oxidation enzymes and co-enzymes and unhindered action of the energy producing mechanism's carbonyl group. The diet and its riboflavin content, as well as the freedom from oxidation inhibitors as selenium requires comprehensive attention. Trace metals that serve the oxidations command their position too, and here copper is important for phenol and amine oxidase activity.

Oxidation hindrance is seen long before a neoplasm appears. The general toxemia with its pre-growth symptoms that generally affect the nervous system and skin more or less than a decade before the growth comes, and the general loss of oxidation power as seen in the sudden increase in taking on fat, the general weakness and easy fatigue, and the hemolytic changes are characteristic. Besides there is the deterioration of the family from generation to generation with a shortening of the pre-growth toxic period and an earlier advent of the growth until it comes before puberty, and the line is extinguished. Steadily increasing inactivation of functional carbonyl groups throughout the body paves the way for the local weakness that yields to the

carcinogen, and the multiplicity of factors that promote and are favored by carbonyl deficiency cannot escape the careful notations of the case record. (Koch, Cancer Journal, Oct., 1924.)

The problem was to invent carbonyl compounds of highest dehydrogenating power, and that was easy. But to secure active free radicals in a state that would serve transportation was not so easy; and to prepare a peroxide free radical of useful type without exploding, and which would stand up for a useful period in aqueous solution was most difficult of all. Facilities in Brazil made the last achievement possible. So it is now demonstrable that each type of reagent has its place in the chain of events required for explanation of the normal procedure and for the correction of the abnormal.

Carbonyl groups are able to prepare their own field of action. Since the value of dehydrogenation depends upon the use of molecular oxygen to form the peroxide free radicals that continue the curative catalysis, carbonyl groups had to first get rid of the intercellular and intracellular colloidal gelation, and even vascular colloid gelation that blocked oxygen transport and caused the essential anoxia. This gelation is due to the action of the amines produced by the fungi always present in the neoplastic lesion, and carbonyl of high activity does inactivate such amines. Where its activity is unhindered no such fungi can take root either, so cancer cannot exist there either.

The symptoms of the recovery process that show a repetition of the symptoms of the pathogenesis is in reverse order, suggest a fragmentation of the pathogen as via a depolymerization, with oxidation of the fragments and energy passing to the host cell at levels from which energy was taken from it during the pathogenesis. Thus it appears from the clinical side that the specific symptoms of the disease and of the cure are due to energy passage from host cell to pathogen during its production and energy passage from the pathogen to the host cell during the cure, and for each symptom complex the energy passed has a special or specific level or quality.

That viruses may polymerize to larger units is suggested not only by the variety of measurements reported, but by the

type of addition they make with the host cell, a free radical double bond affair during anoxia. Indeed they may add to each other under similar conditions and be responsible for a series of disease pictures as stated before. Energy taken from the host cell may build up the pathogen's vital processes and cause death to the host cell, but the pathogen may pass the energy on to the host cell mitotic mechanism and thus cause uncontrolled cell division or neoplasia. To be taken from the host cell at all, it must have some place to go, that is it must pass into some acceptor, as a chemical process that supports some specific function or polymerization; and it is taken and used at specific levels. This accounts for the specific symptoms of the pathogenesis. The return of the energy to the host cell because of oxidation of the pathogen, will affect its functions so far as it has mechanisms to accept the energy. Otherwise it is lost as heat, and that is exactly what we observe during the recovery process. The energy transfer can easily be pictured as conveyed by fluorescent photosensitization, and we look upon this as a normal process in biology generally.

CHAPTER IV

THE REAGENTS

THE TYPE OF REAGENT

It is evident then from the foregoing that two types of attack may be made. One is to destroy whatever carbonyl respiration a pathogen may have, by condensing its carbonyl group with a highly activated amine as a destructive pharmacological measure. The other is to restore the carbonyl function to its highest physiological value in both the pathogen and in the tissue cell. We found that the first procedure not only injured the host cell, but brought about a resistant mutation in the pathogen. Further, as no carbonyl function was evident in viruses, or of note in cancer cells, such therapy must fail there. Observations with trimethyl melamine (Koch, J. Lab. Clin. Med. 1; 299, 1916) demonstrated a refractoriness to a second dose which we interpreted as the basis for the resistance mutation. We therefore prefer the physiological procedure of establishing high carbonyl function which proved its ability to secure separation of a virus parasite or a toxin after integration with the host cell, and also of making it harmless, and possibly biologically useful as well.

In the atrophic types of integration the results include the full freeing of the host cell of integrated toxin or virus. On the sensory side, this was observed in the cure of optic nerve and retina atrophy. On the motor side, by the cure of long standing paralysis and atrophy of Anterior Poliomyelitis, the restoration of function in the cure of the cardiotropic type of aftosa, and the nervous paralysis of rabies and of well established dog and cat distemper. In the neoplastic cases, the cure of cancer of the usual varieties affecting the vital organs with widespread infiltration and metastasis, the reconstruction of destroyed areas for function as speech, the ability to give birth to children, and the return of good stomach, liver, bladder and intestinal action. The recovery process follows a definite pat-