RECAPITULATION AND EXTENSION

Periods of reduced oxidation catalysis result from exhaustion through overwork, exposure to cold, the action of lytic toxins, and from chemicals which like alcohol, ether and other narcotics requiring more catalyst to mediate oxidation than they produce, and from polymerizations of free valent early sugar degradation products induced by appropriate peroxides. Any combination of circumstances which depletes the system, or some part of it, of the carrier of the oxidation chain, leaves it incapable of destroying fluorescent materials that gain entrance. Should an appropriately constructed fluorescent molecule thus become adsorbed into the functional or reproductive mechanism of the cells of an organ, allergic effects are to be expected.

The longer the invading material is present the deeper it adsorbs into its colloidal host, and the greater is the difficulty of removing it. Its very presence serves not only as a 'doorway' facilitating the entrance of the same or similar molecules but also greatly increases responsiveness to their photochemic effects. The longer the material is adsorbed the greater are these effects. The impression so made may be so permanent that it is handed down through the germ plasma to the offspring. This conclusion is based upon the very frequent observation that in all allergies including cancer, successive generations in affected families, other things being equal, display not only a progressively earlier incidence but also a more malignant activity of the affection. We also observe that a person or family

afflicted with one form of allergy is likely to be subject to other forms, and in due time to allergy of the most fundamental, primitive cell structure, its reproductive mechanism, as displayed in psoriasis and neoplasia. The precancer period is therefore generally both an hereditary and a personal allergy epoch in which the latter is shortened as the former is lengthened. Cancer tends to come earlier and earlier in life with each successive generation (17). The precancer allergy period may express itself as migraine, neuritis, arthritis, psoriasis or a marked loss of resistance to infection, especially to tuberculosis, and the inability to burn up the unsaturated groups of the fluorescent materials present in the germinative elements of plant and animal seed, and substances that are especially carcinogenic and related in structure in some instances to the anthracene derivatives mentioned above.

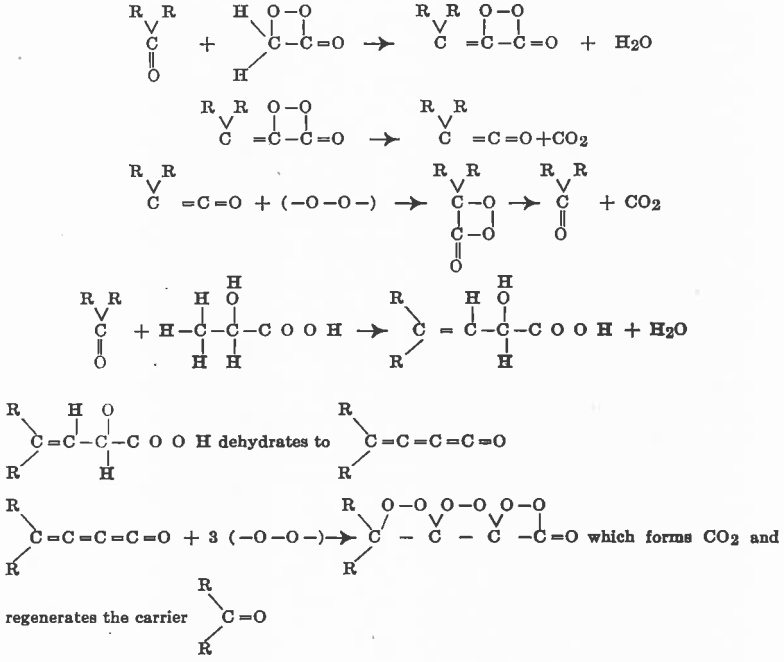
In the anaplastic cell the reproductive mechanism is the only functional mechanism present. Hence it is the only mechanism that can engage in an allergic response so the result of allergy here must be a continuous hyperplasia, so long as the fluorescent agent is present adsorbed in the colloids of the reproductive mechanism, and so long as exothermic reactions are going on in the cell. In malignancy sugar is converted to lactic acid only. The energy so liberated is diverted by the fluorescent agent into the reproductive mechanism where it activates cell divisions. Among known carcinogenic substances, the anthracene derivatives in concentrations of one to a thousand traumatically destroy the differentiated functional mechanism of the cell and produce anaplasia. The surviving more primitive mitotic mechanism responds to the very much weaker concentrations to exhibit neoplasia. All known carcinogenic agents

are fluorescent. The concentrations to which this and other allergic responses are had, are quite minute in keeping with highest efficiency of fluorescent materials. The groups concerned in the fluorescent behavior are the double bonds between carbon atoms and also since the anthracene fraction becomes oxidized readily in the body to anthraquinone, the double union between carbon and oxygen of the keto group thus produced plays its part in the fluorescence. Both sets of double bonds must be considered in the building of a competitor for the energy diverted by the fluorescent allergenic agent. Since the malignant cell carries the burning of sugar only to the lactic acid stage and the oxidation chain is broken at this point, the energy evolved that should normally have gone into the construction and activation of the "hot" molecules of the carrier is absorbed by the fluorescent agent and diverted into the mitotic mechanism where it activates cell division. Therefore no energy is available to produce the carrier and the oxidation process has to stop at lactic acid. Likewise the fatty acids of the affected cells are not fully burned, characteristic fatty changes resulting. The correction of the triple fault in the cancer cell then is to be made by supplying the normal oxidation carrier in a highly active form. The structure of each carrier as presented above serves best of all in every respect, for it is the most active molecule possible possessing the two types of unsaturated groups needed to competitively absorb the exothermic energy liberated in the cell in the production of lactic acid, and thus divert energy from the fluorescent agent to its normal direction in sugar and fat oxidation. Secondly, it behaves as a photosensitizing catalyst, an activator of reactive oxygen, through which the free valences of the fluores-

cent agent are saturated and its allergenic structure destroyed. The one corrective agent therefore destroys the allergenic offender, and restores a normal chemistry in the allergic or malignant cell. The total etiology is therefore removed and normal function restored.

The energy secured through fluorescence from lactic acid production not only activates the reactions of the colloidal structures that serve as acceptors, but in case the fluorescent substance is an anthracene derivative it also activates the "nine" or "ten" positioned carbon atoms toward their oxidation to keto groups thus producing anthraquinones and these groups are thereby activated to react with the hydrogen atoms of the end carbon of lactic acid producing a side chain. The energy of oxidation evolved in these steps is at hand to activate the dehydration of the thus combined lactic acid moiety whereby the anthracene group becomes possessor at the "nine" or at the "ten" position meso-carbon atom of a side chain of three carbon atoms the last united with oxygen, and all unions made with double bonds. Such a group in the presence of the activated oxygen liberated must become immediately saturated therewith and burn to carbon dioxide, restoring the anthraquinone keto group, which becomes reactivated because of its fluorescence as in the first instance, or through the energy evolved, to again combine lactic acid and proceed through the chain reaction again and again. Thus the fluorescent substance serves as a carrier of a chain reaction where deeply adsorbed into the colloids of the functional or reproductive mechanism, it causes an evolution of energy that further forces the acceleration of the function of the cell mechanism affected (34). We believe the activation of a virus is accomplished by similar mechanisms.

With (RR) representing the radicles comprising the rest of the substituted anthracene moiety, the keto group is here represented as reacting with ketene and with lactic acid to carry the chain reactions described. Again the entrance of the normal oxidation chain carrier into the field removes the whole pathogenesis by re-establishing the normal oxidation of sugar and by the destruction of the fluorescent agent through oxidation of its unsaturated fluorescent groups as described above.



The allergenic fate of lactic acid in the way here described need not be the primary factor in carcinogenesis,

but since feeding lactic acid to cancer patients has, in my observation, definitely increased the rate of development and degree of malignancy of cancer, it must be active through a definite fundamental process.

The re-establishing of the normal oxidation chain presents an additional means of destroying the unsaturated groups of the fluorescent agent. This is through the nascent hydrogen atoms liberated when the carrier glyoxylide or malonide and the ketenes add peroxide oxygen. The hydrogen atoms thus set free from hydrogen peroxide or its equivalent may, under suitable conditions, saturate the double bonds of the fluorescent agent and produce a non-fluorescent structure and thus end the pathogenesis.

The importance of the quinone group demands further discussion since all carcinogenic substances known today are able to be oxidized to quinones, and since the natural estrogenic hormones that are carcinogenic already possess quinone structure. Since this is the most destructible group in the molecule and since both the hormone and carcinogenic activities depend upon a constant supply in normal or forced dosage respectively, one must conclude that the quinone group is worn out during activity and is essential to both the physiological and allergenic behaviors. For estrogenic action alone the quinone group may be replaced by a keto group in another set-up, since it has been observed that unsaturated alpha ketonic acids as furalpyruvic acid are estrogenic (29). For continuous allergenic action, however, the quinone keto group should be preserved in a molecule of good stability. Thus, where the meso-positions of anthracene bodies are both changed to quinones, rupture of the molecule is easy and the durability needed for carcinogenesis does not

exist. Where one meso-position is held by an appropriate alkyl group, however, the other meso-position can take on quinone change and the molecule remain quite stable, and, hence, substances of this type like methyl cholanthrene and 3:4 benzopyrene are most actively carcinogenic, we believe.

Para-amino-azo-toluol is not carcinogenic while ortho-aminoazo-toluol is (21). The former cannot readily form a quinone, while the latter can at the para-position. Thus, the importance of the quinone group is again suggested. Aside from the matter of stability, the presence of oxygen in the molecule, in excess of the one quinone group, should contribute properties that are inhibitory to its serving as the carrier of the allergy reaction now under discussion. Plain methyl anthra-quinone and the meso-quinone of several acridine compounds might be studied with profit. The side chain of cholic acid can form a ring with a quinone group at the point of closure and thus cholic acid becomes a substituted quinone of cholanthrene. Whether cholic acid serves as the forerunner or waste product of a hormone serving the cell division of body growth, sex activity, or after this function is inhibited or exhausted, the growth stimulus for neoplasia must still be worked out.

Since carcinogenic substances do not produce cancer until a considerable period has passed after the exposure is made, the possibility is strong that the substance used is not active as such, but only after it has been changed in the body. The spectra of the substances used, therefore, need not be identical with those of the immediately carcinogenic form of each substance. But all cancer producing substances so far known and studied, so far as I am

aware, absorb at three different identical ranges. The difference in absorption of any much more active substance from that just mentioned should very likely point to the change that goes on in the body to make any of them more immediately carcinogenic. Since the oxidation mechanism of the body is able to produce a quinone change at one or both of the meso-carbon atoms of the anthracene series and, should one meso-position be well protected by an appropriate alkyl group and the other take on quinone change or should the quinone change occur in the "8" position, it would seem that the form of the substance best suited to serve as carrier to the allergy reactions, here described, has been accomplished. Stigmasterols of plants offer possibility of quinone change at C-3 and allergenic properties.

The normal energizing of cell division need not be very different from the allergenic procedure thus pictured. Indeed, the keto groups of guanine and xanthin, belonging to nucleic acid, may well behave in the same way as the keto group of the quinones just described. Guanine and xanthin may react with the lactic acid under high pressure to supply the energy for the required reproduction. As this takes place the purine body is oxidized to uric acid which is inactive and thus a limited cell division results and allergic behavior is forestalled. It is not unreasonable to expect the major product of fatigue to serve in this way, in the capacity of a hormone to mediate cell reproduction for the purpose of adapting a tissue to the work it has to perform. In this sense then, lactic acid is not only a key substance in the production of energy for work, but it also provides the energy for developmental adaptation of tissue. Since the cancer cell is hampered also

by a fatigue chemistry, lactic acid may directly serve cell division without the mediation of an allergenic substance, except as this substance keeps up the supply of lactic acid in the way described above. Since narcotics increase the lactic acid in the blood, they should be avoided like dietary lactic acid, fatigue, and worry if a rational regime is to be pursued therapeutically.

Only one more topic in pathogenesis need be introduced. It concerns the x-rays and radium. Fortunately, much able effort has been devoted to the study of the effects of irradiation on matter which cripples the atom by loss of electrons from its nucleus and necessitates a migration of electrons toward the center. The biological influence is appreciated clinically through the fatality of x-ray burns and x-ray cancer. But there is another side to the subject. We must not be content to simply understand the x-ray influence spectrographically as an element spectrum that disregards the state of the element, be it atomic, molecular, ionized, or colloidal. We must look for the effects matter exerts on radiation since x-rays cause cancer, and shock or stimulate cancer cells. Matter definitely affects x-rays or gamma rays in two significant ways. There is the Compton effect which we may compare to the Tyndall effect, and also a sort of fluorescence resulting from the absorption of the rays by matter. The secondary radiations emitted as scattered light when a beam falls upon finely divided matter are of the same frequency as the primary beam, but this is not so in the case of x-ray or gamma rays. Here the angles of collision of the primary beam and electrons will determine the amount of energy expended upon the electron and transformed into motion plus or minus, (elastic collision associated with recoil of the electron) and also

the loss of energy and hence of frequency of the scattered rays leaving the electrons. Thus frequencies differing from those of the primary beam are set up. This is done entirely independently of the chemical nature of the scattering medium, and successive collisions so reduce the frequencies of the secondary, tertiary, etc., scattered beams that the wide range of frequencies produced stand a chance of covering certain specific absorption rates found in living material. But this is not all, another phenomenon takes place that must not be overlooked. It is the production of secondary x-rays from the primary beam of x-rays by the absorbing medium. This effect is comparable to the fluorescence of ultra-violet or visible light, since the nature of the secondary x-rays is determined by and characteristic of the absorbing medium, and is very different from the primary beam. Each scattered ray mentioned above as well as the primary beam may give rise to such 'fluorescence' and not only produce anaplasia as a necrobiotic influence but also a mitogenetic influence directly. Since x-rays carry latent neoplastic effects, carcinogenic materials must be produced within the cell structure possibly from such substances as cholic acid and its relatives and the sex hormones, or analogous bacterial products or nucleic acid compounds which continue the effect from one of transient radiation to that of the most stubborn of carcinogenic changes. X-ray cancer when not envolving too much of the body has been repeatedly brought to normal by the ketenones; so fundamentally the pathogenesis rests upon a crippling of the normal oxidation mechanism, and the defect can be made good by the re-establishment of the normal oxidation catalysis. This is illustrated by a few case histories reported below. It

has also been found that a patient under treatment with one of the ketenones may have the recovery hastened if a few flashes of X-ray are given. Thus momentary x-ray activates the action of the oxidation catalysts and so we may understand whatever beneficial effects irradiation has been able to secure in malignancy to be due to this effect. Unfortunately this disease exists upon a basis of abolished or greatly reduced oxidation catalysis so the danger of totally destroying any possible traces of this essential catalytic agent in the cancer cells and in the body more or less generally is alway present, and it accounts not only for the ultimate increase in the degree and ravages of malignancy, but also for the terrific neuritis and constitutional breakdown of x-rayed patients that have come under our observation. One should, therefore, give serious consideration to the scattering effects and the secondary radiations caused by the tissues and look upon radiations as the richest field of study of carcinogenesis.

We know practically however that the Ketenones do reduce sensitivity to radiation and sometimes cure its most profound effects,—x-ray cancer. So it is possible that they mediate an oxidation of the changed substances which otherwise would hamper the normal cell chemistry, and thus they establish normalcy. They restore a normal cholestrol metabolism and normal nerve function. So it appears that my explanation of impulse conduction on the basis of fluorescence (page 34) may be correct. Here the wave of increased electrical potential accompanying the impulse identifies the brief phase of energy absorption by the fluorescent substance just previous to its transfers to the next molecule.