

**THE CHEMISTRY OF
NATURAL IMMUNITY**

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BY

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"Cancer and Its Allied Diseases"

REVISED EDITION



BOSTON

The Christopher Publishing House,
Boston, U. S. A.

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PRINTED IN THE UNITED STATES OF AMERICA

DEDICATION

This book is dedicated to the many physicians throughout the world who have contributed to the clinical success of the work, meeting difficult clinical problems with diligence, and an adverse professional situation with courage. It is dedicated also to all those who have established chemical, physical and biological data upon which the healing arts must depend for progress.

INTRODUCTION

The time for clear thinking and plain speaking about cancer is long overdue. That cancer is an hereditary disease is a theory held by many who have devoted much time and outstanding ability to the study of the problem.

When a physician first sees cancer in his patient, that patient already has produced children and, more often than not, grandchildren. Therefore, wherein the disease is an hereditary one, the use of surgery, radium, and X-rays, and these three alone, as curative agents against the disease as a wide problem, must forever prove futile. And, organizations using the slogan "The Control of Cancer" to note the special character of their activities, but limiting their therapeutic measures to Surgery, radium and X-rays, must some day expect to be examined as to whether they are, in effect, correct in ignoring the skilled assistance of thousands of general practitioners.

That the condition is environmental in cause, and local in nature, whereby surgery, radium and X-rays can meet the whole field of therapeutic requirements has been proven doubtful, since the death-rate for cancer in New York State, for instance, has risen from a basic figure of 63 in 1900 to 131 in 1934. (*Bulletin, July 1937, American Society for the Control of Cancer.*)

Every comprehensive and sincere treatise on the cancer problem, sets out one Fact, a Fact that is of

more importance than all the ingenious and contentious theories as to the hereditary or the environmental etiology of cancer, or surgery, radium and X-rays which have proven helpless, in attempting to control the disease as a whole. The Fact of such outstanding importance, is the Fact, that advanced cancer in its major forms has disappeared without treatment, sometimes. This Fact should direct all future research for a satisfactory medical treatment of cancer. I myself have seen the spontaneous and complete regression of a severe type of the disease. From that time on, I realized the cure of cancer by medical measures, while unexpected, was within the bounds of possibility, and a thing earnestly to be solicited. I had not dared to hope to see this in my own time, but that it has been well begun, those who read the book can see for themselves; and while of the utmost importance, it is but a part of the therapeutic progress described; and the method of treatment is readily usable.

Well versed in the printed disparagements of Dr. Koch's work, it was with a heavy heart that I first set out to visit him. I resented spending the time which must be taken from my own practice in order to do this, for that year had been the most industrious and the most profitable in my experience. Bluntly I asked him if he could cause the disappearance of cancer, sufficiently often, to make it clear this was caused by his treatment. He assured me he could do so, inviting me to return as often as I desired and to follow some cases through their recovery period. I adopted his suggestion, going to his clinic often, following up cases I had seen treated, and learning from personal observation that he was helping cancer, in a fashion unmistakable. His records were abundant, correctly kept,

and through the months I found they were never altered or falsified.

Always he wished to give his discovery to humanity, and he desired the co-operation of others in improving what he had so well commenced. Therefore it was with his consent, and for this purpose that I took Honorable Forbes Godfrey, M.D., Minister of Health in the Government of Ontario to meet Dr. Koch, and to observe his work.

The first visit lasted three days, and three months later we both returned. For the next two years he went himself, somewhat frequently. He took supplies home with him, and used the treatment in the homes of his own patients. He was thrilled by what he was observing, and profoundly stirred, when this diligence in following up the actual work, enabled him to arrive at a decision, and gave him the right to hold an opinion. He expressed his opinion, that radium did not offer any promise of solving the cancer problem, while praising the merits of the Koch treatment, and he strongly opposed the purchase, by the government, of a supply of radium. He had a clear right to his opinion that the Koch treatment had outstanding virtues, since he had seen recovery of several cases of cancer during its use, and he was happy to announce, "Repeatedly Dr. Koch has stated he is willing and desirous of revealing his formulas to medicine just as soon as his treatment has had proper investigation and endorsement by a medical body." (*Toronto Star*, April 21, 1930.) This was the position he maintained as Minister of Health through a general election which the government won, he being re-elected in his own constituency.

In that part of the Province which might be described as near the Premier's own riding, there was a mining

property being developed which was reputed to contain a large deposit of radium ore of such high grade, that one of the directors is quoted as saying: "We are hopeful that in this deposit is a radium supply large enough for the needs of Canada, and possibly the whole Empire." (*Dr. G. E. Richards, head of the X-Ray and Radiological Department of Toronto General Hospital in the Toronto Star, September 29, 1930.*)

Whether from failing health, or from this combined with his opposing the giving of any government promise to purchase large supplies of radium from the Ontario mine being developed for the patriotic purpose that the whole Empire should be supplied from this source, we find Hon. Forbes Godfrey was relieved of his duties and powers as Minister of Health shortly after helping the government win the election.

When the constituting of a Royal Commission to investigate the cancer problem was being discussed in the Legislature of Ontario, Hon. Forbes Godfrey criticized the usefulness of radium in the treatment of cancer, and maintained the solution of the cancer problem could never be attained by the use of radium, but that on the other hand, the Koch treatment, which he had studied and used for over two years, was of real promise in this direction, and furthermore he could produce several satisfactory cases to support his opinion. The cat was out of the bag.

The then Minister of Health, Hon. John M. Robb, M.D., had never been in close personal contact with Dr. Koch, nor had he observed the effects of the treatment, like his predecessor in this office had done for two years; but he was able to put the cat back into the bag without receiving a scratch, and this is how the trick was accomplished. He said: "I may say

that the Department of Health looked into this method used in cancer treatment in Detroit, and the Detroit Academy of Medicine, Michigan Health Boards and other bodies have informed the Department that it was not a cure for cancer. I am telling the House this to let them know it has been investigated." (*Mail and Empire, Toronto, Canada, April 2, 1931.*)

The Royal Commission was constituted, travelling for months in the United States and Europe, to find out what offered the best hope for a more successful Governmental resistance to cancer, which Honorable Dr. Robb said "Was a public health problem." (*London Free Press, April 2, 1931.*)

This Royal Commission terminated their journeyings by visiting various places in Ontario for the purpose of hearing what ideas individual members of the profession could offer. They came here to London, when on October 1st, 1931, I corroborated what Honorable Forbes Godfrey had said, by showing a variety of cases which are alive today; and I formally offered the gift of the Koch formulas to the Department of Health of the Government on that occasion. Honorable John M. Robb chose to accept contradictory information, written by undisclosed officials of Michigan medical boards, in reply to letters forwarded to them by unnamed members of the Department of Health of the Government. The Honorable John Robb who had popped the cat back into the bag without a scratch was in no way disconcerted, as we have seen. When the Royal Commission issued their report, (*Report of the Royal Commission on the use of Radium and X-Rays in the Treatment of the Sick, etc. Printed by order of The Legislative Assembly of Ontario Sessional Paper No. 41, 1932.*) my

demonstration and offer of gift of the Koch formulas was dismissed with a line and a half; thus: "Dr. David Arnott appeared as the advocate of the use of Koch's serum which he employs in the treatment of cancer." I had pointed out how necessary for truth and accuracy the treatment should not be described as a serum. A full page was devoted to "some original views about cancer" (*Pages 34 and 35 of Report.*) held by Dr. Thomas Lumsden, Director of Cancer Research Laboratory, London Hospital (England), which suggested the possibility and desirability of treatment along lines which I showed them had been put into successful action in London, Ontario.

However, the following "Conclusion" is set out on page 102 of the Report:

"That many investigators are engaged in experimentation seeking the cure of cancer along the lines of serums, tissue extracts and bio-chemical processes. All these methods are in the experimental stage, but there is ample basis for hope that from these or from similar investigations a cure will ultimately be found. The Commission advises the Government, through its research department, should investigate any of these methods of treatment which give reasonable promise."

I have been informed by a member of the Royal Commission that the "Conclusion", "there is ample basis for hope . . . a cure will ultimately be found", was based, insofar as it applied to human beings, almost entirely upon what I presented to the Royal Commission.

Like most family physicians I have been quite competent to recognize the major forms of cancer. This general ability of the family physician has been acknowledged by all "cancer authorities", when they have abused

us through the use of the lay press, for not exercising our powers with proper diligence when we have left our cancer patients till "too late" for the surgeons to use curative measures. If these critics have been sincere, why have they operated on those cases they have known to come "too late," and from the terrible toll of life taken, how can surgery be termed a "cure?"

The abuse of the family physician for not bringing cancer cases early enough, has its parallel in the earlier and still earlier recognition of cancer by microscopic diagnostic methods demanded; and so greatly have the pathologists been pressed, that W. L. Robinson, M.B., Pathologist, Toronto General Hospital, Assistant Professor Pathology, Toronto University, has written: "At other times the variation from normal is so slight that one forms his opinion almost by intuition." (*J. C. M. A.*, September, 1934, page 300.)

How many surgeons earning \$100,000 yearly, have based their claims for having successfully treated cancer, upon the microscopic examination of a piece of tissue, done by an unknown technician, who performs this work for very small pay! An abstract taken from *The American Journal of Cancer*, February, 1937, selected for that Journal by Benjamin R. Shore, M.D. (one of the abstracts' Editors) deals with this question rather well:

"The pathologist should surely have the right to see 'in vivo' the material he must later study under the microscope and he should have something to say too, about the selection of the material to be examined, and even the best method of securing it if the surgeon's methods seem inadequate. Only the inexperienced operator thinks that he can put a nickel, or less, in the pathological slot and emerge with a diagnosis which

he can accept without question." (*The Pathologist's Part in Malignant Disease from the Surgeon's Point of View*, U. Maes. New Orleans M. & S. J. 88:543-546, 1936.)

The exclusive right to make the diagnosis by surgical procedure, assumed and held by the surgeons should terminate. "A biopsy is the examination of a piece of tissue removed during life. In his Beaumont Foundation Lectures, Ewing says that 'the resort to a biopsy is a confession of failure, due to clinical inexperience or lack of data from other methods of diagnosis'." (*Text Book of Pathology*, by Boyd, Page 337, Second Edition.)

Now if the family physician and the laity themselves are to be held responsible for the recognition of cancer before it becomes inoperable, they also can recognize it when it has reached the far-on stages and subsequently been controlled by the Koch treatment.

The most bitter and abusive critics of Dr. Koch are those who never have followed a series of cases treated by him, as Honorable Forbes Godfrey and I have done; and it would be unwise, ever to allow them to control the manufacture and distribution of the therapeutic reagents, which he discovered and developed.

On the other hand, steps should be taken which will provide the Koch treatment for large numbers of those now regarded as hopelessly stricken.

To help bring about such useful service to humanity, I have devoted a great deal of time, during the last eleven years; and in turn secured the co-operation of the late Honorable Forbes Godfrey, of whom it was written in commenting on "the thoroughness of his investigations" (*Toronto Star*, April 21, 1930) that, "we have yet to hear any one say he was not a first

class doctor. He has an experience as a general practitioner which we doubt could be duplicated by half a dozen men in Canada. He is also remarkably hospitable to new ideas. He was the first of his profession in Toronto to administer diphtheritic antitoxin serum, and publicly admit it. His declaration took place at a meeting of the Ontario Medical Association. He was sternly rebuked by the late Charles Sheard who told him that a man doing such a thing should be arrested. But the confident young Mimico doctor stood his ground and said that the day would come when doctors not using the serum would be arrested." (*The Mail and Empire, Toronto, July 13, 1931.*)

It was this personal experience which, when I first went to him, enabled the Honorable Forbes Godfrey to recognize my history of Dr. Koch and his treatment was both truthful and accurate.

Circumstances had forced me to begin the clinical use of the Koch practice in cases other than cancer. Elsewhere I have outlined specific instances of outstanding success in treating cancer, non-malignant tumors, tuberculosis, acute and chronic infections, as well as allergies (*Natural Immunity?*) Let me report some cases of special significance, in the field of allied diseases, so clearly pioneered by Dr. Koch in his "Cancer and Its Allied Diseases."

J. K., aged 12, appeared in my office with "Shingles" of considerable severity. The lesions then had been in evidence for three days, and she had not slept for four nights, owing to the sharpness of the pain which accompanied her trouble. The pain was relieved soon after the treatment was administered, and it never returned. She slept the first night following the injection of the Glyoxylide, and the next day the blisters

stood up on a perfectly normal colored background; and the whole thing disappeared in eight days.

This little patient, always had been a problem; and for six years the use of small doses of thyroid extract had been observed as necessary to meet her constitutional deficiency. Her thyroid function became normal after the Koch treatment was administered, and has remained so. All the physical, mental, and character improvements such change might produce, did result, and have continued.

Here a long arrested thyroid development had been restored, and it has continued to provide all normal requirements.

The "Shingles" gave visible evidence of posterior nerve damage. As though by word of command, the symptoms and physical signs turned towards normal immediately after the Koch treatment had been used, nor was there any hesitation in progress, once this course had become apparent.

With such dramatic control of posterior nerve damage, it was obvious that anterior nerve trouble found in Infantile Paralysis, might give a favorable response to the treatment, also. A fortnight later it was put to the test in an apparently dying patient, then already paralyzed four days. The result in this case was marvelous, the first favorable signs being in evidence within ten minutes. (*Natural Immunity* page 119-120.)

A patient of mature years, suffering from phlebitis which had extended the length of her leg up to the groin, causing her such pain she was unable to endure putting her foot to the ground, was not making satisfactory progress, though active treatment by the use of ordinary measures had been employed during the

month she had been confined to bed. The Koch procedure caused an early relief of pain, and a rapid recession of the visible signs of the trouble. In a fortnight she was almost completely restored.

At the same time, several fibromata which had been established in her right arm for several years, reduced in size till they had completely disappeared.

She had been treating for cataract of both eyes, awaiting the time when operation might be resorted to, that she might not be permanently blind. It was six months before I had the courage to enquire as to her vision, and was delighted to find it, too, had been so markedly improved she was able to see to sew at night without difficulty or distress. A check-up by her optician disclosed she had better vision, both for reading and for distance, than she had experienced during many years previously.

There was a feeling of great satisfaction whenever I had been able to confirm Dr. Koch's recorded successes in what to me were fresh fields of therapeutics. He encouraged me, gave me an absolutely free hand, showed me the methods he used in preparing the Glyoxylide, and allowed me to cherish the notion that I had helped to break a bit of new ground, myself. At last there came a night when I was glad I had thrust ahead.

In December, 1936, my brother, a family physician like our father before us, was suddenly stricken with a most terribly severe seizure of coronary thrombosis. Morphine relieved him only as it made him unconscious, and it left the harmful effects of repeated, large, hypodermic doses of the drug, while it had contributed nothing towards his recovery. The use of Glyoxylide was followed by considerable relief, and it was repeated in three and a half days, after which the coronary

pain left him completely, and has not returned. A careful convalescence was observed, for the severity of the attack had been most far-reaching in its harmful influence. However, for some months now, he has been able to drive his car on long trips, walk briskly, and lead a life free from discomfort which might indicate any return of his sickness.

My brother and I resent the fact, that the continued claims of surgery to domination in the diagnosis and treatment of cancer, successfully blocks the use of the Koch treatment in coronary thrombosis, often called the "doctors' disease."

Dr. Koch! My brother and I salute you.

Pasteur, ignorant of surgery, radium, or X-ray treatment, disclosed to the world a new and definite knowledge of the cause of many serious diseases. This discovery of bacterial infection gave nothing in his day with which to cure disease once it had been established. His knowledge was, and for the most part continues to be applied to the preventing of disease, through using isolation, antiseptics and vaccines. Over a period of years it has become recognized that persons equally exposed to bacterial infections, exhibited widely differing degrees of susceptibility. This mysterious difference lies deep within the human body. Who would dare attempt the tremendous stride required to pass from knowledge of visible bacterial invasion, to that of unseen, general body defenses, and lend a gentle, helping hand where sorely needed?

The text of this volume by Dr. Koch, deals with definite bio-chemical changes which occur in the body before bacterial invasion takes place to produce well-known acute and chronic diseases. This bio-chemical change has been discovered by him to consist of a

faltering of the oxidative mechanism—the most fundamental chemical process connected with life. In an important percentage of cases, it has been readily restored to normal, by the using of the reagents discovered, developed, and described by Dr. Koch.

His treatment is a specific therapy, directed towards restoring a most profound vital action, to higher efficiency. Were we logical we would expect, not one but many evidences of benefit to our systems, where the treatment has been applied successfully.

Those possessing broad, practical experience with the treatment, such as the late Honorable Forbes Godfrey sought and achieved, know full well this does happen.

Medical research begins with the need of studying the unknown. The first stages are secret because unimportant, even academically. This is true of all new laboratory and clinical work, and the more so, should progress be attempted by individuals who are not affiliated with some institution endowed with large sums of money from either publicly or privately supplied sources. The co-operation of the entire medical world should be mobilized in the war on cancer and no longer should we tolerate the study of cancer exclusively by laboratory workers experimenting with mice, nor permit surgery and radiology to monopolize the treatment of the disease, thereby blocking promising efforts in the far wider field open to the general practitioner into whose hands serious problems generally fall.

It was my idea that the Koch treatment might best be put to work through the services which are provided by the Department of Health of the Government of Ontario.

After several years effort along these lines had been exerted, it became evident that no early, favorable action need be expected; and as his book, "Natural Immunity" was taking form, Dr. Koch went to Europe, hoping to find some men of highest scientific attainments, experienced in cancer research, who would be able to repeat and confirm his work.

Professor J. Maisin, of the Cancer Institute, University of Louvain, Belgium, for many years a leader in cancer research, was chosen from those he was able to meet.

Professor Maisin has confirmed Dr. Koch's work, and this association, which began in the Fall of 1934, still continues.

During the years Dr. Koch felt requisite for the maturing of his observations and conclusions sufficiently to justify publication, he was persecuted for using a secret remedy. The production of "Natural Immunity", with its enlightening chemistry, only increased the abusive comment from those leaders recognized as well-practised in destructive criticism.

His first discoveries affected a situation of academic interest only when he succeeded in identifying the lethal poison which developed after the removal of the parathyroid glands, which in those days had been taken out, sometimes, during operations for goitre.

For this achievement he received well-merited praise; the editorial in the *Journal of the American Medical Association*, closing with: "in any event the final successful isolation of recognized toxic chemical products of traceable origin has paved the way to definite conceptions and specific lines of enquiry where hitherto the explanations have been vague and the outlook unpromising."

You will find this has been quoted from Volume 61, Page 1049 of the *Journal of the American Medical Association*, September 27, 1913, and the genius for succeeding in research thus noted twenty-four years ago, has accomplished so much in the field of cancer, that, were the words quoted above used now in this connection, they would be entirely inadequate for the purpose of describing the progress he has made with this problem.

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AUTHOR'S FOREWORD

It might be taken as a rule that where sugar is vigorously burned in physiological processes, not only are fats burned too, but also every other combustible substance that enters the blood and tissues. Natural immunity destroys every virus, every disease germ poison, or structure, and every allergenic agent in this way. To force immunity to disease, therefore, one can do no better than to establish a vigorous oxidation mechanism. The present day understanding of this process is not sufficient to be of much help, and to work out the different steps that are traversed in the oxidation of sugar will take some years of additional effort. The dilemma was even worse twenty-five years ago when the problem came across my path. It was useless to think of clarifying the oxidation process step by step in the short time at my disposal. So instead of studying the sugar burning mechanism directly to learn what deficiencies might happen in the process to break immunity, I thought it more practical to ascertain what types of atomic groupings could exert toxic effects, and to identify them with different stages in sugar oxidation. In those days photochemistry was not developed to the point where it could be of much help, and besides, disease toxins were not recognized by their atomic groupings, but were regarded as protein molecules of quite large molecular weights and no one would see any relationship between oxidation and immunity. Lysins, precipitins, and agglutinins

were the rage. However I was strongly attracted by the possibilities of such unsaturated bonds as join the imid group of guanidin to the carbon atom, and occurs in histamine, and also by the double bonds of the ethylene group and between carbon and oxygen in the keto and particularly in the quinone groups. Personal experiments with fluorescent substances gave two startling disclosures; one, a substance that can produce allergically a sensation that continues for days after application to the skin, even after it is washed off. This substance is a halogen compound related in structure to caffeic acid, coumarin, and æsculin, thyroxin, and adrenalin. The other experience was the production of a faint blue light for a while by a mixture evolving exothermic energy in the presence of a fluorescent substance. It was in the attempts at explanation of these phenomena that the systems of sugar oxidation and the idea of allergy and immunity presented here were worked out. That the cancer abnormality is associated with the failure to utilize lime appears from the following facts. In cancer there tends to be a lipoid in water phase of colloid dispersion. Such conditions exist experimentally in water lipoid systems according to J. Loeb where there is a dominance of monovalent over divalent cations. In the case at hand it appears that calcium utilization is deficient. Calcium is certainly necessary to sugar oxidation, and the calcium fixing vitamins and hormones all are helpful in cancer treatment in my experience. Even powdered chalk is helpful. Calcium, phosphoric acid, and guanidine are lost in the urine after parathyroidectomy. Guanidine fits into the oxidation mechanism in two places and in connection with phosphoric acid utilization. Phosphoric acid in

anærobic glycolysis as occurs in cancer, appears to aid in hydrolysis toward lactic acid production with the aid of coenzymes and calcium; but in the ærobic burning of sugar I believe that it mediates a dehydration of the hexose molecules in several ways that will be described later. This dehydration permits direct peroxidation and burning of the molecule; and thus calcium deficiency and oxidation block run hand in hand in cancer metabolism. The calcium, one might conclude, plays its part not only in the dehydration and peroxidation of the straight and cyclic chains of more than one carbon atom but also in the utilization of and peroxidation of the formaldehyde produced from the straight unsaturated chains during their oxidation as described below, and particularly in the synthesis of unburned formaldehyde into the diketone described later, and even into hexose. At least this theory comes close to the basis of the present research. If it is in error, as well might be, the error is lucky indeed for through it we arrived at a useful treatment of otherwise incurable disease; and the recoveries are able to be permanent as twenty years of practical application now shows.

In the following discussion, photochemic definitions closely follow the wordings of Griffith and McKeown, "Photoprocesses in Gaseous and Liquid Systems," Longmans, Green and Co. Colloidal affairs are described in MacDonagh's terminology because of its familiarity to physicians. This does not mean that we agree with MacDonagh's thesis entirely; for instance, it is impossible to understand how the blood protein can vary in quantity to the enormous extent that the scarcity of particles in some microscopic fields and the large number in others in the same and different

humans would indicate. It would seem that the blood protein is represented by the homogenous material between the particles as well as the particles themselves, which possibly are artifacts produced by the contact with foreign conditions attending microscopic examination. The type and extent of artifact produced will be an index to colloidal stability or entropy and thus, though it does not represent the total blood colloid, it gives an estimate of conditions. We therefore follow MacDonagh's descriptive system trusting that the reader will permit our use of the terms according to this explanation. We might add that the lipid changes he describes in cancer should find better explanation in Loeb's expositions of water lipid systems as influenced by monovalent and divalent cations and by anion variations. The lipid deposits in cancer cells are definitely the result of the inability to burn them, and therefore they depend upon the deficiency in and the crippling of the oxidation catalysis that forms the basis of our subject. Essentially the subject centers about the activation of oxygen by the free valences of the extremely labile metabolites of aerobic glycolysis on the one hand, and about the polymerization of and inactivation of these valences on the other, when oxygen supply is inadequate and stable peroxides of high molecular weight are present to favor polymerization. The allergenic diversion of energy, and the changes in colloidal and cation distributions that have the greatest clinical importance are dependant matters. Primary in my experience stands the inhibitory effects of amino and imino groups against the free valent activity of the carbonyl and ethylene groups in their catalysis of the oxidations as I describe them here.

The Chemistry of Natural Immunity

PERTINENT STATEMENTS ON OXIDATION

One would expect that the cell structure that controls compensatory reproduction and hypertrophy would be the same structure that plays the fundamental part in the functions of the cell. It appears that this is exactly the case for the site of energy production is really the surfaces of the nucleus granules or genes. The energy production by the nucleo-protein complex is therefore important to our subject. The distribution of the energy throughout the conduction, secretion, contractile, or reproductive mechanisms from the energy generator, the nucleus, is likewise important to our subject, and since we conclude cholesterol is essential to this function we must look into the changes it undergoes. Though the material thus introduced reaches far out into the subject of physiology, we will try to keep as straight a path as possible in describing their essential position in, and such of their processes that constitute immunity to toxic activity of various origins, and to demonstrate how when this immunity is exhausted, the malfunctions that constitute allergy come about. The main purpose is to show how the natural immunity mechanism may be restored and the infection or the allergy, be it simple as in asthma or

profound as in malignancy, may be overcome and normalcy again be established.

The fact that the cell nucleus is the site of oxidations for energy production has been recognized a long time. My own observations on this were made in connection with some experiments on the parathyroid glands twenty-five years ago when I found that various guanidine bases were excreted in the urine after parathyroidectomy, during and previous to the violent muscle activity of tetany. Because of the presence of guanidine in the guanine unit of nucleic acid and the general extensive nucleolysis and cytolysis that followed parathyroidectomy its excretion in the urine might have resulted from excessive activity and breakdown of the nucleic acid structure, and thus it gave suspicion of being an important unit in the oxidation mechanism. Now a days we know that guanidine plays an important part in the oxidation of ammonia, via citrullin arginin and ornithin. Its place too in creatine phosphoric acid is important for the phosphorylation of adenylic acid; and adenyolphosphate is essential to anærobic glycolysis. This was not known twenty-five years ago. Still it is not peculiar that one should have suspected the guanine sugar phosphoric acid nucleotide to belong to the energy producing mechanism for cell functions, and that it's contained guanidine therefore should be an important structural unit. Most important structural units are toxic when excessive in the blood stream; even calcium is. It is shed in large quantities after parathyroidectomy and also plays an essential role in sugar oxidation. However we must not think of the parathyroids as simple calcium guardians. It is generally thought that the blood calcium and the phosphate of the blood

bear a constant relation to each other. Their product in milligrams per hundred cc. of blood is about 36, so when the calcium excretion is raised the phosphate excretion drops and vice versa. But after parathyroidectomy both the calcium and the phosphate increase in the blood and are excreted in greatly increased amounts in the urine, so the situation is not simply a matter of deficient calcium retention. Indeed the calcium may increase in the blood after parathyroidectomy even to the extent of its toxic depressant action. All of the toxic substances secreted in large quantities during the early tetany stages while the kidneys are still functioning, can be washed out of the blood by various saline injections with relief of tetany, but they accumulate during the late stages when the kidneys cease functioning, when neither calcium solutions nor other solutions are able to allay the toxic state. Indeed then, calcium injections produce coma more quickly. At this stage the glomerulæ of the kidneys are completely shot by way of hemorrhagic degeneration. If the parathyroid glands simply controlled calcium metabolism the tetany could be completely controlled and none of these conditions would arise. The difficulty with the "total calcium function theorists" is that their parathyroidectomies were not complete and the unremoved tissue had a chance to undergo compensatory hypertrophy. Complete parathyroidectomy is always fatal. Calcium deficiency is controllable. This digression could be followed further. The various other toxic bases, histamine, decarboxylated arginin, and other bases which I have not yet had opportunity to identify, point to the most extreme demands for oxidation energy during tetany because these bases are decarboxylated tissue structures

that are sacrificed for even the little energy yielded by their decarboxylation. So even the parathyroid function has its influence upon the oxidation mechanism.

The progress of the evolution of the oxidation mechanism, which, too, must undergo change with adaptation, should permit the operation of several contemporary mechanisms; namely, that being developed, that being discarded, and perhaps a middle course mostly in use. It is known that in the hepatectomized animal fructose is not used by the tissues, and glucose is used. Yet glycogen is split by the liver to fructose di-phosphate which is directly usable by the tissues. Fructose is not used as such and fructose di-phosphate is not known to circulate in the blood. However the white blood cells that have much to do in carrying material after a meal may manufacture or may well convey some precious fructose phosphate compound from the liver to the working cells where it is liberated under conditions of tissue activity. This consideration permits that a dehydrated hexose molecule be burned for energy production, and a demand upon white cells which may call them into hyperplasia when their work is handicapped. Thus we have employed a large dehydrated fructose phosphate and glucose phosphate molecule and their fully unsaturated derivatives in the leukemias, coronary thrombosis and cancer, and in the acute infections as poliomyelitis and in the chronic infections like tuberculosis and leprosy that excite a small round cell infiltration, with the most pleasing results. And since the deficiency involved is repaired by this procedure we believe our reasoning has been correct.

Finally, any deficiency in any of the accessories to

the oxidation process may contribute to the pathologies dependent upon impaired oxidation. Vitamins A, B, B₂, and D, Warburg's yellow pigment, ascorbic acid, cytochrome, adenylic acid, and the other co-enzymes must all be considered and made good wherever cell multiplication goes on beyond physiological control, or as we may say "allergically." However at the bottom of such conditions stands the toxic structure we will discuss later and this must be removed through a vigorous oxidation catalysis. It is even necessary to maintain the balance of mono-valent and di-valent cations necessary to correct the injury to dispersion of the cell colloids caused by physiological activity, such as happens in an extreme degree as a result to changes in complex substances in the development of tetany. Therefore calcium, magnesium, and potassium are required in correct amounts in various oxidation systems, to maintain a water in lipid phase.

The other subject of importance to normal and allergic cell function is the conduction mechanism, for the energy produced on the surfaces of the chromatin material must be distributed to the functioning structures in amounts exactly required by the demand for each functional activity. Two facts are observable. Striations are seen under high magnification to lead from the surfaces of the chromatin material to the contractile, secretory, and impulse-conducting mechanisms. It is known that every nucleated cell contains sterols and only cells with organized nuclei do. Sterols are synthesized in the body. They are fluorescent substances that can absorb energy from exothermic reactions going on in their medium, whereby they enter a new state which can only be retained a very short period, the energy being immediately dissipated.

as radiation or handed on to an absorbing chemical system of correct absorption and emission spectrum range and in which this energy is spent in activating its chemical processes. Moreover where molecules are attached or arranged end on end, as they are known to be in fibril formations, every condition exists to pass the energy absorbed by the first molecule on to each successive molecule until it can reach an appropriate acceptor for this energy, the functional structure. In cancer where the cholesterol chemistry is so badly upset that the blood concentrations may rise high very sharply or drop below the normal with equal speed most irregularly, it is evident that this substance is not efficiently occupying its place in the cell structure and is produced very irregularly. The ease of hydrogenation of bonds of "C-5," its sensitivity to radiation and the occurrence of several cis- and trans-isomeric forms about the saturated "carbon atom 5" and involving the active hydroxyl group, and also the readiness with which other cyclic and side chain carbon atoms may become unsaturated leaves it open to a great variety of changes under the influence of photo-active substances and agents, in an energy producing medium like the living cell. Changed structure may even promote altered molecular arrangement and destroy the straight fibrillar structure so that the energy is no longer conducted to the functional mechanism but remains in the nucleus to activate its function of cell division. Oxidations in the side chain lead to the formation of poisons resembling the heart poisons produced by some plants and animals. These changes need not take place, yet in view of the cachexia of cancer and the fact that sclerotic calcification cholesterol vascular changes are lessened by malignancy, the

study of cancer is not complete until all of the changes undergone by cholesterol are settled.

Even though it is chemically possible to produce every known sex hormone from cholesterol, it would be difficult to prove that this is their parent substance in the body. I believe that it is and in the transformation the hydroxyl and unsaturated bonds of "C-5" remain, and the side chain of the five membered ring is oxidized away leaving a keto-group at "C-17." The keto- and hydroxy-groups may change position with hydrogen added at "C-17," producing a strongly oestrogenic substance with marked stimulating action on the growth of the genitalia of rats. If both positions are occupied by hydroxyls the effect is less on genitalia development, but stronger in changing the growth of the cock's comb. When both these positions are occupied by keto groups the effect on the growth of the genitalia is increased. The most active of all the male hormones has the keto group at position "C-3" and the hydroxyl group at position "C-17." With these shifts the position of the unsaturated bonds vary about "C-5." Although reduction of the keto group to hydroxyl increases activity in some respects, this may be referable to the easy oxidation of the keto group which may reduce its concentration in the blood before it gets to work on its chosen apparatus, whereas the hydroxy derivative on oxidation becomes a nascent active keto group at the site of its activity and is thus protected until it is used. Thus the comb is a special accessory sex organ adapted to one function only and oxidation of the hydroxyl groups is not adding much to its activity; whereas the genitalia have other work to do along the usual physiological lines and here the "keto" formed hormone should serve

more acceptably. Possibly in this way the apparent inconsistency is made reasonable. At the same time not only the importance of the unsaturated bonds associated with "C-5" is emphasized, but also the carbonyl group which is able to mediate a chain reaction liberating energy according to the mechanism discussed later on. Except that the ring A becomes aromatic and photo-chemic activity is thus increased, the same situations hold for the follicular and corpus luteum hormones.

The vitamins of the D series, sterols closely allied to cholesterol, have essential physiological activity. Their photochemic significance and relation to calcium retention without parathyroid aid gives their sterol structure still more importance. This is especially true since calcium is necessary to the sugar oxidation mechanism. Through photochemic action the provitamin, ergosterol, is changed to a three ring system having three sets of conjugated double bonds between carbon atoms. The A ring is ruptured at "C-9," and the hydroxyl is retained at "C-3." An unsaturated carbon linkage is present in the side chain. Photochemic activity is therefore marked. There is no proof that the vitamin is not changed in the tissues by oxidation either at the hydroxyl or in the side chain to resemble a sex hormone more closely. The fact that only the structure with a free hydroxyl unprotected by an acetyl or glucoside union is active is significant in this direction. It is interesting too that the anti-rachitic and the calcium-fixing properties are separate, and the further products of irradiation of ergosterol, tachysterol, and toxysterol have no anti-rachitic properties like vitamin D, calciferol, although they are strong calcium fixing agents.

Substances of such essential and complex physiological behavior as the three sterol groups mentioned may well be related to other bodies of somewhat similar structure that possess profound influence on the chemistry of living tissues. Thus certain benzanthracenes and even simpler aromatic compounds which I believe inhibit the dehydration and peroxidation of hexoses are able to remove karyokinesis and cell division from the normal physiological control and place neoplasia in the category of allergies as I view them. This property is due to specific fluorescence to a large degree and also, I believe, to the ability to produce a carbonyl group that serves as the carrier of a chain reaction which will be described later.

The oxidation mechanism includes very definitely also both vitamins B₁ and B₂. Vitamin B₁ is a Thiol-pyrrol-pyrimidine derivative. Its molecule contains five unsaturated unions between carbon atoms. Its structure suggests possibility of being a pro-nucleic acid derivative, and its function is tied up with that of the nervous system. Its deficiency causes beri-beri, a disease showing peripheral neuritis and paralysis, suppressed heart action, and diminished oxidation with lactic acid accumulation in the brain. Pyruvic acid accumulates in the blood, and brain tissue slices use less oxygen than normal brain slices. Addition of the vitamin to the slices immediately raises the oxidations to normal and its administration to animals showing deficiency immediately corrects the total pathology. Thus this vitamin is definitely an oxidation agent. It may function thus directly by virtue of its several unsaturated unions between carbon atoms and between carbon and nitrogen atoms. It possesses an amino group that can very easily be replaced by an oxygen

atom thus producing a carbonyl group able to serve as an oxidation carrier. It may also serve the oxidation mechanism indirectly as a building unit for the production of nucleic acid.

B₂ the anti-pellagra substance is probably a flavine derivative containing five double bonds and two carbonyl groups and a pentose attached to a meso-nitrogen atom in nucleotide fashion. Thus it resembles Warburg's yellow pigment, a hydrogen acceptor in the presence of dehydrogenase co-enzyme. If the structure so far suggested is correct this body too functions in the oxidation mechanism, which its carbonyl groups may serve as carriers.

Thus the vitamins fit into the body chemistry much like the hormones and may replace them in some respects, for instance, tachysterol parathyroid and suprarenal hormone are interchangeable in calcium fixing activity. Moreover, under natural living conditions where a man exercises and perspires in the sunlight, he manufactures his own ergosterol (which otherwise is only built up in fungi and fish), and he converts this substance into vitamin D, and its further calcium-fixing irradiation products. But excessive irradiation may contribute carcinogenic properties.

Other substances of the highest physiological importance are products of digestion of aging spermatozoa absorbed from the seminal vesicles. They improve the efficiency of muscle and nerve cell function. The amount of adenylic acid and other nuclein digestion products may not be large, but the efficiency, perhaps of some particular structure formed with the aging of the sperm is important to muscle quality, and to mental activity, and also to the oxidation mechanism in a way that improves immunity to infection.

The chemistry of these substances is unknown at present, but their importance will call for their full investigation some time.

That physiologically important metabolites may become dangerously toxic is observed in the behavior of acetyl-choline, which is produced at the nerve ending of the autonomic system during their function. This substance is highly active in a dose of one to ten million, and to it some are ascribing the cause of such vascular disease as coronary thrombosis and occlusion. It is known that acetyl-choline is formed constantly at the parasympathetic nerve endings, and in worried or the high-strung people there is some chance for its accumulation. However, this could not take place in anyone with an unimpeded oxidation mechanism. Choline has much to do with the oxidation of fats. That it prevents the conversion of amino acids and of sugars to fats under the influence of cholesterol, it seems there is sufficient evidence when the rest of the oxidation mechanism is normal. It does not aid the burning of aceto-acetic acid, but where the rest of the oxidation mechanism is sound, its presence favors the burning of fats or their precursors by another route. It is, therefore, an important link in the oxidation mechanism, but of course where the oxidation process is otherwise impaired we must assume that it not only fails to function and therefore accumulates or is formed in greater quantity for compensation than normally occurs; and worst of all it is not burned itself and produces its toxic effects. Thus one might well assume that it is a factor in coronary disease, much like cholesterol is in other vascular degenerations that are so well known. In fact they both accumulate where the normal catalysis of oxidation is broken, and there-

fore both coronary disease and atheromatous degeneration and arterial sclerosis depend upon one basic deficiency, a crippled oxidation catalysis. Toxic blood colloid jelling is a commanding factor. That this is true will be seen from the fact that recovery is promptly brought about by the oxidation catalysts discussed below. Moreover in advanced arterial sclerosis with tortuous nodulated pipe stem vessels recovery has been accomplished with full restoration to normal so far as symptomatology and palpation could reveal. Vascular normalcy is important to tissue function and obliterative vascular disease so often the cause of tissue degeneration that one might say that all disease shows its marks on the vascular system early or late. The infectious granulomata all start out with an obliterative endarteritis. Cancer does also, and cancer should be classified with the granulomata. They are all based upon toxic activity that destroys oxidation catalysis. They are all curable by restoration of the oxidation catalysis to normal or to better than normal. This holds also for Renaud's and Berger's diseases.

Through an over-active nervous system, therefore, in the presence of deficient oxidation catalysis, an accumulation of metabolites to toxic concentration, be it choline, neurine, cholesterol or some other, is possible whereby disease is produced in a similar way to that caused by disease germ poisons where the oxidation catalysis is insufficient to destroy them. The various allergies including cancer possess in this way an additional mechanism for being brought about and being maintained. Again let me repeat that the restoration of a vigorous oxidation catalysis removes the

offending substance, no matter what its origin may be, and thus establishes the basis for recovery.

The oxidation mechanism is also influenced by the glands of internal secretion. They all play a part in conserving or stimulating fuel and oxygen usage in a variety of complicated ways which adapts their service perfectly to the most specifically differentiated requirements. For their best co-ordination they are placed under the control of the central nervous system. Under normal conditions this is a wise provision, but it lays the gland system open to allergic interference through the nervous system. Since they mutually antagonize or reinforce each other's activity, allergic hyperactivity of a part of the nerve center may excite or inhibit one or more gland activities and produce profound changes such as diabetes, toxic goitre, or any of the other well known or obscure endocrine disturbances. Fortunately allergic activity of nervous tissue (for example, as expressed by shingles, or even certain forms of mental imbalance and inhibited development) is readily corrected by the measures we propose farther along, and thus the most profound endocrine disease has yielded very promptly and permanently to this treatment. Such prompt response could only follow the correction of an allergic state for it takes place sooner than tissue regeneration of any gland could be accomplished. However, the nerve or the gland tissue development that follows the removal of oxidation inhibition has been observed to take place with remarkable speed; for instance, the descent and development of the testes in young adults, and the gain of normal painless menstruation cycles in young females, the restoration of thyroid and

pituitary function, and the improvement in mentality of imbeciles and idiots.

An experiment that shows the control exercised by the central nervous system over endocrine function is that where the circulation from one dog (B) was sent through the brain of another (A) whose brain was otherwise not receiving blood from his body, nor was the blood of the donor animal (B) circulating through A's body. When the blood sugar was increased in B's blood flowing through A's brain, tests of his (A's) systematic blood showed a drop in blood sugar and when the blood sugar in B's blood was decreased, A's systematic blood showed a rise in sugar. It is known, too, that gastric ulcer develops mostly in those who have suffered some form of nerve exhaustion or other change in the central nervous system. A mental or a nervous influence is a factor in many allergic disturbances. Adjunct to the brain control, the pituitary exercises hormone control over the other ductless glands, and allergic activity of any of its functions like allergy of any of the endocrines demonstrates characteristic disease.

The chemical structures of the hormones so far isolated and producible synthetically possess strong photochemic possibilities and both adrenalin and thyroxin contain hydroxyl groups in their aromatic rings that can easily oxidize to keto groups. The sex hormones have already been discussed from this standpoint.

There are several metabolites that may also share oxidation function; one, so well known in connection with allergy, histamine, deserve a word. Its imidazol ring, when present in the normal amino acid histidine, plays an important harmless role. Simple

decarboxylation of this amino-acid gives the molecule very toxic properties and the ability to produce allergic necrosis. The mechanism is not understood; conjecture leads to the photochemic properties resident in the unsaturated groups of the imidazol ring which in the decarboxylated molecule may exactly annul the vital activity of its parent substance. The instance is valuable in emphasizing the profound effect so slight a change as the loss of a carboxyl group may cause. Since a tissue hampered by poor oxygen supply or poor oxidation catalysis will sacrifice its vital structural elements, amino-acids, for the energy secured by decarboxylation as my parathyroid studies have shown, allergic necrosis may thus depend upon a crippled oxidation mechanism.

The tissue slice method has facilitated the study of the oxidation mechanism in a most gratifying way and the facts so far revealed in the mechanisms of anærobic glycolysis are quite illuminating. However, the normal oxidation mechanism as conducted in the body with adequate oxygen supply must indeed be entirely different. One fact, the presence of free phosphoric acid, settles the matter. The system of sugar oxidation proposed later is very different from the usual conceptions. It was worked out over twenty-five years ago, long before any of the co-enzyme systems were established. The scheme is not intended to exclude any accessory to the mechanism but to fit in the general procedure the best it may.

One must not forget the ease with which some aromatic hydroxyl compounds change to quinones, or even exist as both forms in equilibrium in solution and in the solid state. Since as we will describe, the quinone group can conduct chain reactions and liberate

energy quite perpetually, and through its fluorescent properties this group is like other unsaturated unions between atoms and can appropriate exothermic energy evolved in its environment and either use it for activation of its own chemical processes, or hand the energy on to a suitable acceptor that can so use it, we have in these properties all that is necessary to make a virus of a suitably constructed molecule.

The change of hydroxyl to quinone in the sterols is also accompanied by changes in isomerism and as we have seen definite alterations in the growth promoting properties follow. The stigmasterols, the sterols occurring in plants, must also function with the genes for differentiated activities and for reproduction, and most likely, as I have suggested, in the distribution of the energy generated at the nuclear surfaces. Changes in structure of the type under discussion, other than takes place in normal metabolism, must pervert function and therefore both the plant and animal foods submitted to chemical activities in preserving processes of modern civilization, or through the action of drugs and anæsthetics taken into the body should be investigated as possible causes at the bottom of the cancer situation.

Through irradiation by sunlight, X-rays or ultra-violet light or by chemical activity the production of double bonds and the shifting of those present to produce isomers not normally present, the normal oxidation and conducting functions we assign to cholestrol may well be lost to be replaced by catalytic peroxidation activities such as the terpenes carry on. Thus one molecule of altered cholesterol adsorbed in chromatin becomes the energy generator that is in position to force the chemistry of cell division of neoplasia. The

cholesterol changed by irradiation and oxygen has also some opportunity to take on quinone structure and become a catalyst for energy production by the method to be described later, which energy in like manner must force cell division. Polymerization of unsaturated derivatives of cholesterol and from sugars offers a group of substances not yet known to exist but which must not be forgotten in cancer research, and the stigmaterol peroxides in ether extract of wheat germ oil showing carcinogenic behavior must be examined from that standpoint too. Twenty-five years ago when this work was started the chemistry of the sterols was almost a blank page, so the chemical properties thought essential to carcinogenic activity could not be identified with them, and indeed they need not be the only important materials of this class. That there are plenty others should have become evident from this survey.

It might be argued that all substances that have to do with energy production and energy distribution are of sugar origin, though greatly modified, or carry sugar in their structures. Among them ascorbic acid deserves a word. It is definitely of sugar origin, derived by oxidation of two carbon atoms. The reduced form carries an unsaturated union between the second and third carbon atoms. The oxidized form carries a chain of three keto groups, two of them hydrated. It is able therefore to carry an oxidation chain reaction, and has definite photochemic properties. Since it is so easily destructible it is able to serve in a minor way in the immunity against infection and against cancer as described below, and the reason for the feebleness of ascorbic acid as compared with each of the various Ketenones we use for this purpose is observable

on comparison. These reagents were put into use a quarter of a century ago. It is, therefore, a matter of the greatest satisfaction that the chemistry of vitamin C, so recently contributed, is confirmatory to our thesis.

With this general survey of free valency activities as an introduction we may go on to the changes in catalysis we ascribe to the causation and correction of lost natural immunity.

The study of allergy and immunity as here presented proceeds on the basis of the established experience of physiochemistry and physiology with the aid of a working hypothesis and clinical observations. It identifies a defect in oxidation catalysis as a fundamental feature in the causation of disease, without which secondary causes should not find support.

The treatment outlined follows as a logical development and since it removes a primary cause, the many disease manifestations that characterize the activity of dependent secondary causes cease to exist where it operates. The pathogenic feature is traced to the specific physiochemical properties resident in atomic free valency existing in appropriately constructed molecules. Thus in one chemical property general to a large number of chemical compounds, highly specific photochemic activity is recognized because of the special architecture of the molecule concerned. The unit of atomic arrangement fundamental to specific pathogenesis within a large clinical field is the subject of our thesis therefore; and it is discussed here as concisely as possible. The work was started about twenty-five years ago. The first divisional report was made in the Medical Record of New York in October, 1920.

THE CHEMICAL BASIS OF ALLERGY

Working Hypothesis

Allergy or the hyperactivity of any cell function such as secretion, contraction, generation of nerve impulses, or cell division, not under physiological control, is the result of the photosensitizing action of a fluorescent substance adsorbed into the colloidal surfaces of the functional mechanism concerned, whereby the fluorescent substance directs the energy liberated by the usual exothermic reactions going on in the cell into the functional mechanism adsorbing it, and here this energy activates or accelerates the chemical reactions of this function. Thus the hypersecretion of hay fever, the spasms of asthma, or the increased cell divisions of neoplasia are instituted and maintained, and in the same manner other allergic activities are brought about (15). Most of the diverted energy is evolved in the hydrolysis of glucose to lactic acid, amounting to 270 calories per gram of lactic acid produced. Conversion of necrobiotic rays to mitogenetic rays through fluorescence is an important possibility in the gumma, leprosy, and tubercle. Very little energy need be diverted to maintain certain forms of allergy, especially an allergy of the nervous system. Here one cell group continuously generating impulses, which traverse a train of neurones associated in one concept, establishes a fixed idea, a second personality, a neurosis, or a delusion of insanity. In the same way the activation of viruses is also made possible.

Fluorescent substances (1) are able to absorb energy either of radiation of certain wave length or the energy

liberated by exothermic chemical reactions in progress in the medium where they exist. In so doing they become a second system, which, owing to their limited storage capacity, reverts to their original state immediately giving up this energy, either as radiation of lower frequency or as chemical energy without degradation, if the fluorescent substance happens to be held intimately adsorbed into the surfaces of a reactive substance capable of serving as an acceptor of this energy. In this case, the energy received activates or accelerates the chemical processes of the acceptor. A fluorescent substance behaving in this way is called a photosensitizing catalyst. In order to serve in such capacity, both it and the acceptor must be able to absorb energy in the same spectrum ranges at a different range from that at which sensitization takes place, at which latter range only the sensitizer can absorb energy. The positions of atomic groups with unsaturated valences, with reference to the most reactive atoms of the molecule, determine the spectrum sensitive regions characterizing the substance. In the case of the carcinogenic anthracene derivatives, (2) (3) the '9' and '10' 'meso-positioned' carbon atoms are most reactive and oxidize readily to keto groups. On this basis it happens that of the four different dibenzanthracenes only that with benzene rings occupying the 1, 2, and 5, 6, positions possesses correct spectrum absorption and emission qualities to be moderately carcinogenic. The 3: 4 benzopyrene molecule and cholanthrenes with appropriate meso-substitution are more and more energetically carcinogenic as their spectrum characteristics, or that of their quinones, coincide better with those of the mitogenetic mechanism of animal cells. One is tempted to predict that radiation of the living cell with their energy qual-

ities will result in hyperplasia. The crucial matter is that the fluorescent substance can take up energy evolved in exothermic reactions and be so changed that it emits this energy as its own characteristic emission spectrum. Thus the specificity of absorption of both sensitizer and acceptor exist at a different energy level from that at which the sensitizer absorbs the activating energy it passes on to the acceptor. To exemplify such photoactivity one might mention the "phosphorescence" of decaying vegetable matter, the light of the firefly, whereby excess energy of rapid muscle contraction is emitted as light which otherwise would accumulate as heat,* and the "cold light" displays where a fluorescent substance takes up energy from an oxidation reaction and emits it as light, also the sensitization of the gelatin-silver-salt complex of the photographic plate to red light by adsorbed fluorescent dyes, or the sensitization of Siloxen to the longer wave lengths by adsorbed rhodamine, and the acceleration of Siloxen reactions, because of its adsorbed oxy-compounds, to the chemical energy liberated as the reaction progresses. In this way in the allergic cell the fluorescent agent also is affected by this energy and as will be seen, the chemical resistance of the system it involves is removed so that it, itself, mediates a chain reaction using lactic acid and oxygen as reactants to evolve energy which also contributes to the allergy. So in two ways, energy for producing and activating the "hot" molecules of the carrier, which should continue the oxidation process beyond lactic acid, is removed. When the fluorescent substance behaves in this way, it serves as a negative catalyst to the oxidation mechanism. Since it re-

*This is my own explanation which I must admit has not been studied experimentally.

moves the energy ordinarily absorbable by, and necessary to, the production of the carrier of the normal oxidation chain, it must contain the same structural groups as the normal carrier. They are both subject to the same chemical reactions, therefore, and absorb energy in the same ranges competitively. This point is employed in building the chemical substances used to destroy the photochemic fluorescent sensitizer of allergy, the negative catalyst, that prevents the production of the carrier of the normal oxidation chain in the pathogenesis of cancer, and destroys resistance to infection.

Since fluorescence depends upon the unsaturated valences between carbon atoms, between carbon and nitrogen, and between carbon and oxygen atoms, and since, according to our views, all forms of allergy depend upon this fluorescence, and the "carrier" powers of the carbonyl group, only one substance, so constructed that it can saturate these valences, is required to overcome all forms of allergy, even including the allergy of the plastic system, neoplasia, and also to destroy virus activity.

Inasmuch as catalysts are active in low concentration, it is important that the reaction by which the fluorescence is removed should bring about a complete removal of every trace of the fluorescent structure. This cannot be accomplished by a reversible reaction such as enzymes mediate. Only a reaction chain in which the fluorescent substance serves as one of the reactants and the treatment measure is the carrier of the reaction could be expected to succeed completely. A brief statement on the nature of chain reactions (1) will explain this point. Their characteristic features are that the reaction is mediated by a "carrier", an activated mole-

cule or atom. This carrier renders the fresh reactant molecules active. The carrier once formed establishes a cycle of consecutive reactions which reproduce the carrier and produce the resultants as by-products of the cycle. High quantum yield results. The chain can only be ended by complete conversion of the reactants or by a destruction of the carrier, and the latter can only be done by processes other than those that maintain the chain. Hence, the last survivor of the chain is normally the carrier which, in the case at hand, may remain adsorbed in the colloids any length of time to reestablish the chain if fresh reactants ever enter the field again. The process then ends in immunity which, I have clinical observations that indicate, may be passed on to the next generation.

Since the anærobic oxidation chain is interrupted at lactic acid production (4) in the pathogenesis of malignancy and must be restored, the corrective measure to be preferred is that structure which reestablishes the ærobic oxidation of sugar and lactic acid and also engages the fluorescent groups in a vigorous oxidation chain reaction. Hence the unsaturated groups exhibiting the fluorescence and activated oxygen liberated in the body are employed as the reactants. The carriers chosen are the structure $\text{O}=\text{C}=\text{C}=\text{O}$, ("Glyoxylide") or less advantageously $\text{O}=\text{C}=\text{C}=\text{C}=\text{O}$ ("Malonide"), the internal anhydrides of glyoxylic and malonic acids, ketenes and the peroxides of form-aldehyde which functions in the same way. They may be grouped because of similar structure under the name "Ketenones." They appear to serve as the carriers of the normal oxidation chain and are employed therapeutically in loose combination with protective molecules or as precursors (peroxides of form-

aldehyde) from which they are liberated in active form in the body. To mediate the oxidation of the fluorescent pathogenic units they behave as photosensitizing catalysts and activate the union of peroxide oxygen and the unsaturated valences of the fluorescent atoms. The determination of their "carrier" structure depends upon an original interpretation of sugar oxidation.

It is based in part upon the influence of the carbonyl group in determining hydrogen shift between three carbon atoms where an ethylene linkage is involved, and upon its tendency to favor formation of an ethylene union between its adjacent alpha and beta carbon atoms. We may thus picture the production of a double bond able to add peroxide oxygen and subsequently split to two carbonyl groups. It appears to me that the degradation of fatty acids two carbons at a time is accomplished in this way and that the conversion of fats to sugars and sugars to fats is mediated by the same phenomenon. It is in these changes I believe, that the iodine of the thyroid and parathyroid secretions catalytically serve the oxidation mechanism, possibly through an oxide of iodine, and that the wasting of tissues by their excessive function is accomplished.

Our catalysts accomplish a cyclic inhibition and hastening of catalase activity either through a polymerization of, or a union with catalase, from which catalase is again regenerated. Various peroxides exhibit this activity when studied spectrographically.

The action of our catalysts may be interpreted as the activation of oxygen through their free valences preliminary to behaving as peroxides in one stage of their activity.

THE OXIDATION MECHANISM

Much has been done in the study of the oxidations, but all is not yet learned. It seems pretty certain, however, that for any particular substance the course followed is determined by its structure and its environmental influences. Moreover, in larger molecules the differences in the various atomic groups will determine a correspondingly different oxidation course. Even the difference in the positions of similar atomic groups with reference to some other very active group will determine a different behavior in each.

In a system as complex as the living cell, one may only provisionally draw conclusions as to the events of the oxidation process from what one is able to observe in vitro experiments, and it is especially hazardous to use the behaviors of substances that do not exist in tissues as criteria. So complex indeed is the living system that one need never expect to exactly reproduce it in vitro to serve any experiment that might be designed. Therefore, the broadest field of possibilities must be selected from to lay out the most likely course of events; and these must all be checked most carefully by known data. Moreover, the rapidity of change in the intermediaries of oxidation of sugar and fats is so great that these substances need not be expected to patiently wait for isolations by any laboratory chemist. Where aerobic oxidation is concerned their order of instability is such that they have escaped detection. This moreover is the field of activity we are concerned with in matters of immunity. The

bodies we describe as intermediaries in ærobic oxidations possess an instability of exactly such an order and I have reasons to feel that what I shall propose here as the most likely mechanism is quite possibly correct.

In sugar all carbon atoms do not have the same values. We might say that quite remotely they all possess different values, and hence the well known optical isomerism is possible. However, certain carbon atoms, that of the carbonyl group and its alpha and beta neighbors, have especially important differences from the rest. Glucose and fructose, because of the difference in position of the carbonyl groups, have especially useful differences. Yet when the carbonyl groups are inactivated there may be sufficient similarity to permit quite uniform dehydrations to take place with the formation of a long unsaturated chain, straight or cyclic, quite able to be oxidized directly to carbon dioxide or simply leave a residue of formaldehyde or its peroxide. Inositol found in muscle may be related to a process such as this.

It is more probable that dehydration, peroxidation, and cleavage of the fructose and glucose molecules are accomplished between the carbon atoms in alpha and beta position to the carbonyl groups. This reaction is catalyzed by iodine. I may add that the same reaction takes place in the oxidation of fats. Both in the sugar and fatty acid so changed, the carbon atoms of the peroxide union yield to the splitting of the molecule and the production of two carbonyl groups. Thus from glucose, a two carbon and a four carbon chain aldehyde are formed; and from fructose one molecule of glyceric aldehyde and one of the aldehyde of glyceric acid are formed. From the four carbon chain two aldehyde molecules are formed. Likewise,

by repeating this procedure glyceric aldehyde may undergo the same change yielding formaldehyde and glyoxylic acid. By continued dehydrations, the glyceric aldehyde, the aldehyde of glyceric acid, the glyoxylic acid, and glycollic aldehyde that were formed are converted into ketenes and suboxides of carbon as pictured below. To indicate their metabolic relations we designate the internal anhydride of glyoxylic acid, $\text{O}=\text{C}=\text{C}=\text{O}$, as Glyoxylide, the internal anhydride of malonic acid, $\text{O}=\text{C}=\text{C}=\text{C}=\text{O}$, as Malonide, the ketene of glycollic aldehyde, $\text{H}_2\text{C}=\text{C}=\text{O}$, is called ketene, and the ketene of lactic acid, $\text{H}_2\text{C}=\text{C}=\text{C}=\text{O}$, is called Lactene or Malonene. We give the whole group the name "Ketenones," for we use them together in one solution for therapy purposes.

These unsaturated substances are extremely reactive in two directions because of the wealth of free valency they possess. They either take up peroxide oxygen and burn to carbon dioxide and water, or first enter a chain reaction, as such or as a peroxide, with suitable structures as pictured below before burning to carbon dioxide and water and at the same time inducing oxidation of the substance combined. They may add water reversing the process, reproducing sugar in any of its forms. It seems certain that the free valency of carbon atoms tends to activate oxygen to what I have called the "peroxide oxygen" state, in which it will combine free valent carbon. Hence, the more active are the free valences of the substance the greater is its catalytic power of activating oxygen. So the free valences of the very unstable unsaturated Glyoxylide, Malonide, and Ketenes with which we are dealing may induce a "peroxide state" of oxygen so actively that it will combine the lethargic free valences of un-

saturated carbon atoms of the large clumsy molecules of pathogenic coal tar products and similar bodies. When hydrolysis takes the place of the dehydrations and peroxidations described above, glycolaldehyde, glyceric aldehyde, and dihydroxyacetone intermediately precede ketene and malonene. All five are active oxidation catalysts since their carbonyl groups are flanked with ethylene or hydroxyl, and not by amino groups.

On the other hand the free valency disposes them to polymerization especially under several environmental conditions that are possibly exaggerated in living cells. When oxygen is not adequately supplied in excess and when thus a minor portion of their free valences are peroxidized, or when stable peroxides are present, polymerizations are not only free to take place, but under the influence of the peroxide present, are even accelerated, so that difficultly burned clumsy bodies are formed that further block the oxidation progress by being present adsorbed in the functional mechanisms of the cell and thus in the way, as it were. The withdrawal of free carbon valences from the field in this way reduces the activation of peroxide oxygen and so also poisons the oxidation mechanism.

It appears that a peroxide oxygen union with carbon either "in parallel" or "in series" disposes to an activation of the electrons of the carbon atoms of the group and by "resonance" also to an activation of the electrons of similarly positioned unsaturated carbon atoms of neighbor molecules because such free valences will unite with each other if oxygen is not available.

Environmental offenders such as excessive exposure to ultraviolet light, especially in the absence of adequate oxygen produces peroxides of various unsaturated bodies of large molecular weight that do not yield to easy oxidation. Thus derivatives of cholesterol, produced in the body by sun light, by bacterial action, by the action of peroxides in anæsthetics taken into the body or contacted in plant pollens or as coal-tar preparations, and also in many "aniline dye" products, form peroxides that polymerize and produce polymerizations of unsaturated metabolites with the significance mentioned here, or yield fluorescent substances that can transfer the energy of any stage of normal metabolism to any functional mechanism affected, and thus through fluorescence activate and force functional activity beyond physiological control. This I believe is the true mechanism of allergy.

Therefore, the unsaturated products of both sugar and fat metabolism as well as of other normal cell constituents may be diverted from their normal service by polymerization so as to cause disease, when the oxygen supply is inadequate to fully burn free valences, and when difficultly burned peroxides are present to help an abnormal polymerization along. Depletion of accessory catalysts like peroxidase and catalase disposes to this abnormal process.

In the oxidation of fats, one might propose that the hydroxyl of the carbonyl of fatty acid and the hydrogen of the alpha carbon atom are removed first, then hydrogen shift from the carbon atom in beta position to the carbonyl carbon takes place so that the ethylene group is formed by the alpha and beta positioned carbon atoms. Peroxidation here with subsequent split leaves two molecules with terminal car-

bonyl groups from which oxidation proceeds again. Thus is explained the well proven metabolic fact that two carbons at a time are removed from fatty acid in its oxidation, and so this scheme seems to fit not only the physiological facts, but to offer the basis of pathologic events exhibited in disease, no matter what direction it ultimately takes.

As age advances the vigor of the oxidations is progressively reduced. In plants the same phenomenon should be observed to follow the complexity in the terpene structures formed, that is, the failure of oxidations to compete with polymerization. In cancer cells the malignancy of the cell and its loss of oxidizing power run hand in hand in my experience and so too the presence of polymers is more notable. One is therefore tempted to conclude that old age changes will ultimately lead to neoplastic efforts in any cell.

This very neoplastic effort of cell multiplication, mediated by fluorescent properties specifically affecting the particular mitotic mechanism of the cells that are involved, offers them opportunity to adsorb from the blood stream and dilute the offending substance to a state of adsorption in which it is more readily oxidized by such oxidizing powers as still survive in the cells concerned. The tendency of a lipoid in water phase in cancer cells aids this detoxication of the blood. Most important and amazing of all, the dilution is directed toward conversion of the polymeres of intermediary unsaturated oxidation metabolites into their monomere, active catalytic form, which when restored should be able to reestablish the oxidation mechanism in the cell. Thus the crucial step in the causation of malignancy is directed toward the cure. Some day when the multiplication is rapid enough as

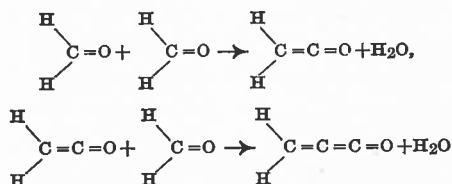
compared with the production of the toxic factor the evolutionary purpose of the whole effort will be realized, and an efficient oxidizing machine will be produced which should serve as a protection not only against malignancy, but also against all of its associated allergic expressions, old age changes, and the lowered resistance against infection. If this anticipated accomplishment of the race will also help the development of the fetus and give the infant the start we observe after treating an expectant mother with our Ketones, then a better race will be brought into the world as well.

Here too is a guide to the active therapy to be enlisted and we shall see later on how dilution of the specific polymers concerned yield the active monomers needed to restore a normal oxidation catalysis and recovery.

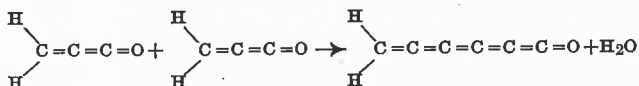
Formaldehyde might be grouped with the ketenes in our scheme of the oxidations in spite of its possession of but one carbon atom. It serves as the carrier of a chain reaction which any of the ketenes may mediate, and it also serves as the starting point for the synthesis of ketene, of lactic acid, and even of hexose and glycogen. This is possible because of the ease of union of two molecules by dehydration that forms double bonds between carbon atoms, able to take up oxygen and burn to formaldehyde and carbon dioxide on the one hand, or on the other, to take up water as the condensations are made and thus to produce the hydrated molecules lactic acid, hexose and glycogen.

Under proper conditions, two molecules of formaldehyde may condense to form glycolaldehyde, and three may form dihydroxyacetone and glyceric aldehyde. Three molecules of glycolaldehyde may condense to

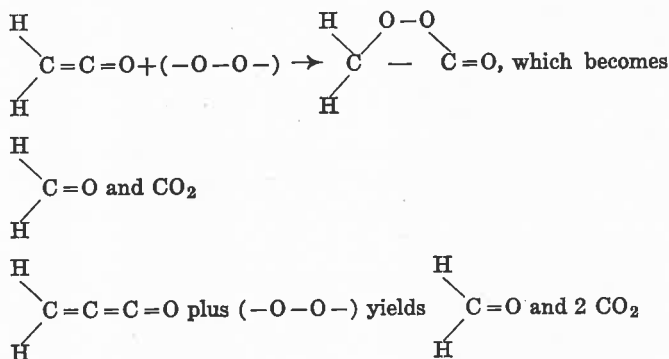
form glucose, and two of glyceric aldehyde may form fructose, as may also occur in plants. I have found these intermediaries to be strong oxidation catalysts



The Malonene or Lactene so formed by adding 2 H₂O becomes lactic acid.



The Hexylene so formed by addition of five molecules of water becomes hexose, (glucose). Ketenes add oxygen and yield CO₂ and formaldehyde.



within the body, able to remove the basis of otherwise incurable disease by correcting an existing deficiency, and I therefore assign to them all an important place in aerobic glycolysis, and natural immunity.

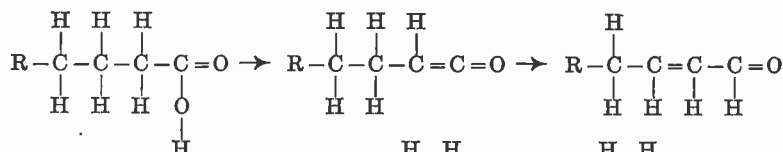
Ketene or Lactene by condensing with lactic acid either before or after dehydration and peroxidation leads to the production of formaldehyde, water, and

carbon dioxide. The dehydrated product of condensation on the other hand may add water to become a pentose or hexose.

Thus energy may be yielded or utilized by the unsaturated carbon chains by oxidation or hydration, and carbon dioxide or sugar produced. The formaldehyde or ketene formed in the first reaction may also be burned or carry another cycle as the conditions determine. Fatty acid may dehydrate and then undergo hydrogen shift yielding double bonds between the alpha and beta carbon atoms which may add peroxide oxygen and split off a two carbon atom chain glyoxal leaving the long chain with a carbonyl group at which oxidation commences the same series of events.

The procedure outlined gains probability because the intermediaries in aerobic glycolysis have never been isolated and thus must share the same order of instability as the substances of the scheme presented here. Hence the peroxides described could never be detected, nor have peroxides been found in the body in view of the fact that peroxidase is well distributed in the tissues. Furthermore, oxidation of the substances here described as paralyzable by such substances as the quinones and dihydroxy-aromatic compounds, which prevent peroxidation of free valences.

The amino group definitely antagonizes oxidation boosting by the carbonyl group. It protects protein amino acids from oxidation. Thus when the amino group is removed from glycine, glycolaldehyde remains to favor oxidation, and when carboxyl is removed from histidine, the lethal inhibitor histamine remains. Acquired immunity then depends upon proteolysis and desamidation to liberate carbonyl activity.



which adds $(-\text{O}-\text{O}-)$ yielding $\text{R}-\text{C}-\text{C}=\text{O}$ and $\text{O}=\text{C}-\text{C}-\text{OH}$ which

$$\begin{array}{c}
 \text{H} & \text{H} \\
 | & | \\
 \text{O}=\text{C}-\text{C}-\text{OH} \\
 | \\
 \text{O} \\
 | \\
 \text{H}
 \end{array}$$

dehydrates to $\text{O}=\text{C}-\text{C} \begin{array}{l} \text{OH} \\ | \\ \text{H} \end{array}$ and yields on peroxidation, formic acid and

carbon dioxide. Thus the chemical basis for oxidation of fats is provided by this system.

The anti-oxidation effects of carcinogenic bodies exhibited in the animal body and observed in isolated tissues by Pourbaix in Maisin's laboratory should possibly be explained as a quinone activity. Commercially the phenomenon is employed to suppress polymerization of unsaturated substances, because the polymerization is catalysed by traces of peroxides, and the aromatic dihydroxy bodies and quinones prevent the production of the peroxides. These facts support my contention that the carcinogenic agents act as quinones and that the normal oxidation process is a peroxidation of unsaturated groups.

Also the desaturated six carbon chains, the phosphorylated hexoses, the adenylic nicotinic acid co-enzyme system, and creatine phosphoric acid all play important roles in maintaining a complete oxidation mechanism and are essential to recovery be the disease leukemia, an infection, some form of allergy, or cancer.

There are probably many more accessory oxidation

agents than the hormones and vitamins mentioned so far. Each has its specific work of limited scope but none appear to be able to accomplish this special work without the support of the general catalysts of sugar oxidation we have described here. This is evident in the fact that serious hormone deficiency, endocrine gland abnormality, and vitamin deficiency on a diet that is not seriously inadequate can be changed to normal by the use of the unsaturated ketones have introduced. From what has been said above it should appear that they play a fundamental role in both plant and animal oxidations, and were it not for their great instability evidence of their existence in alcohol producing plants, the yeasts and moulds, should be forthcoming. The weak immunizing properties of yeast extracts may be attributed to them as well as to various oxidation coenzymes like adenylic and nicotinic acids.

It is interesting that the co-enzymes of oxidation contain carbon and nitrogen atoms joined by double bonds. I should interpret them as having a negative catalytic effect protective against destruction of the co-enzyme nucleus, for these groups both in guanidine and in the imidazol ring may practically completely annul oxidation in very small dosage and bring about rapid tissue death. One means is by inactivating peroxidase and catalase, and thus the decarboxylation of creatine and histidine by tissues forced to secure energy anaerobically compares with the primitive toxic mechanism of bacteria that produce methyl guanidine and histamine from creatine and histidine in colon putrefaction. Since the imide group serves as oxidation carrier in arginine in the oxidation of ammonia decarboxylation may negate the catalysis.

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.

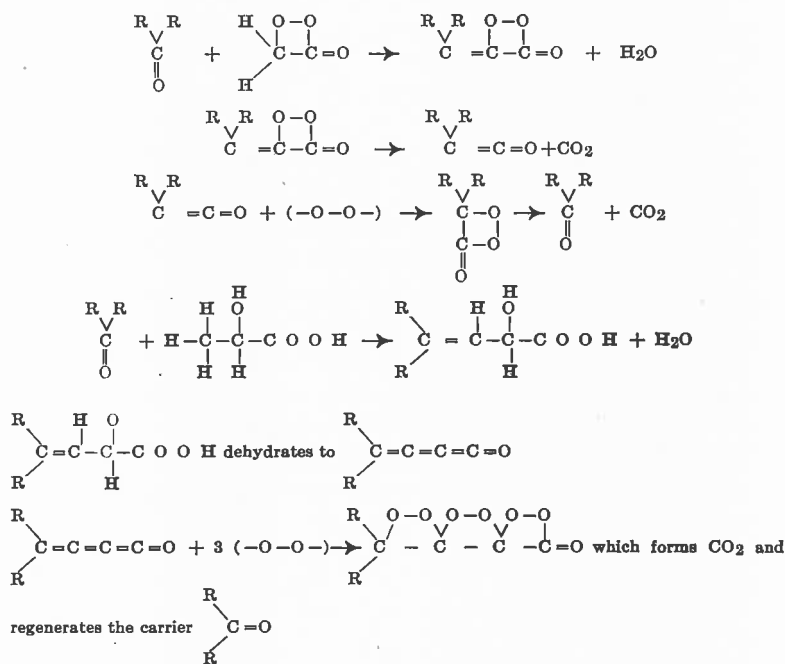
In the anaplastic cell the reproductive mechanism is the only functional mechanism present. Hence it is the only mechanism that can engage in an allergic response so the result of allergy here must be a continuous hyperplasia, so long as the fluorescent agent is present adsorbed in the colloids of the 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 involving 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 always 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 cholesterol 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.

THE PRODUCTION OF THE KETENONES

The search for physiological evidence of the existence of the normal oxidation carrier ($\text{O}=\text{C}=\text{C}=\text{O}$), the internal anhydride of glyoxylic acid, was made in 1917 to 1920, and curative results obtained by the use of tissue extracts in the treatment of malignancy were reported in the New York Medical Record, October 30, 1920 (12). In 1931 (5) and 1937 (11) Maisin reported confirmatory results of organotherapy in cancer. Naturally a substance so unstable as glyoxylide or the internal anhydride of malonic acid could not exist long in aqueous solutions or be isolated as such, but formic and glyoxylic acids were found. It appears that isorrhopsis changes within the molecules of the potassium salts of glyoxylic acid, or formic acid, and of formaldehyde and its peroxide, yield the unsaturated molecule transiently either directly or by the union of two carbonyl groups set free. Clinical utilization of these intermediary substances in the allergies and neoplasia yield identical results to those obtained with the tissue extracts. However, it must be emphasized that neither tissue extracts nor the solutions prepared as mentioned are uniformly reliable sources of the active material. But where conditions are favourable and the preparation process is correctly carried out, the unsaturated molecule is produced with active life long enough to start the chain reaction desired to bring about recovery. When this happens the recovery processes in all instances are identical.

The solutions yield similar spectrographic curves,

moreover, and their identical activity demonstrates that the same active substance is generated even though we start out with different materials in several different ways. "Glyoxylide" is too unstable to be isolated even as a dry gas and can exist in solution only as an intermediary substance during some reaction as stated. Important corroboration is found in recent interpretations of the formula of formic acid by P. C. Ray (7) where, a "lone pair" of electrons is credited to the carbonyl group. He finds that the hydrogen atom attached directly to carbon ionizes to form salts, and that the failure of formic acid to form an anhydride or acid halide like other organic acids depends upon this fact. This behavior is interesting from our standpoint because it explains also that the calcium of calcium formate may form a hydroxide by uniting with the two hydroxyl groups present and thus liberate two carbonyl groups that may unite to form the Glyoxylide. Satisfactory support to the unsaturated structure of the active molecule is afforded by the internal anhydride of malonic acid "malonide" ($\text{O}=\text{C}=\text{C}=\text{C}=\text{O}$) which possesses the same unsaturated groups as "glyoxylide" ($\text{O}=\text{C}=\text{C}=\text{O}$). Both possess the unsaturated valences between carbon atoms and between carbon and oxygen atoms. Both absorb quite similarly spectographically. Both behave in the same way clinically and in the catalysis of oxidation of living tissues in vitro, except that the "malonide" owing to its extra carbon atom is less reactive and less efficient. As we have seen in the foregoing pages it becomes converted into glyoxylide as the chain reaction progresses. Aqueous solution of both unsaturated bodies reverse their structure back to the saturated glyoxylic and malonic acids. For reliable preparations

therefore it is necessary to produce the glyoxylide and malonide by special methods.

The method of extracting the substances from tissues that I used early in this work is expensive and only occasionally successful. Beef heart or brain is taken fresh from the animal and rapidly ground up into three times the weight of ice cold absolute alcohol in which a good quantity of anhydrous sodium sulphate powder was added. Thus the tissue is dehydrated and the protein precipitated. It may stand over night. The alcohol is filtered off and then the residue is extracted with dry ether, several times. The extract is concentrated and precipitated with acetone which extracts some fats and cholesterol. The precipitate is then freed from acetone by vacuum and extracted with ether again. This extract contains the lecithin and cephaline fractions with the metabolites adsorbed. It can be precipitated again with absolute alcohol to separate the lecithin solution from the cephalin precipitate, which carries the largest fraction of the important metabolites. Because of the presence of growth promoting substances in living tissues, or produced by action of the ether upon the lipoids, these extracts may not always be curative. Sometimes they stimulate cancer growth and increase the degree of malignancy.

Several practical means may be used for the production of the catalysts here mentioned. They are being taught to selected groups of physicians. We believe it preferable to give exact training in the technique than to leave so important a matter open to errors that my own experience shows are bound to creep in. The methods in general have been stated in "Natural Immunity," Fourth Edition, issued by the Koch Founda-

tion in 1936. One of the metabolites that is easy to prepare, and which has a wide range of activity in malignancy, the infections, and a few allergic conditions, is the peroxide of formaldehyde. It is prepared by contact of dry formaldehyde gas with dry hydrogen peroxide, dissolved in dry ethyl ether. Since the synthesis is exothermic it must be controlled as to rate and temperature to avoid violent explosion. Dry formaldehyde can be prepared from dry para-formaldehyde by warming it. The ether solution of hydrogen peroxide into which it is lead should be kept ice cold. It is well for the operator to be protected since the reaction sometimes "runs away." The crystalline product should be recrystallized till pure as shown by the melting point. It is then diluted to one to a billion or higher by a technique that is perfect, in every detail in avoiding contamination, as to pure water, air, clean apparatus, clean hands, breath, absence of perfumes, etc. This aqueous solution deteriorates very rapidly.

A dilute solution of formic acid or calcium formate might theoretically at least yield or behave as Glyoxylide; so too an alkaline solution of formic aldehyde and the peroxide of formaldehyde; for in solution both can produce free carbonyl groups momentarily which are free to unite with double bonds. But since their free valences are so unstable they either activate oxygen and become peroxides or immediately polymerize unless some nascent ammonia, iodine, or other radicle is present to saturate the ethylene union. Glyoxylic acid may be assumed to undergo double dehydration and produce the Glyoxylide under colloidal conditions present in living cells. When the peroxide of formaldehyde undergoes internal oxidation of its hydrogen atoms to form a free carbonyl group leading to Gly-

oxylide production, an important catalytic event takes place through the migrations of the oxygen and hydrogen electrons.

In the production of the peroxides of formaldehyde and especially when the "chimney" method with platinum as hydrogen acceptor is used, both the single and double formaldehyde peroxides are formed with some Glyoxylide which soon polymerizes to a yellow and pink liquid and decomposes. The amount of Glyoxylide formed depends upon the amount of air admitted to the reaction system. Of course, other substances are formed too. Of these, glycolaldehyde is most important because it dehydrates to ketene, and because of its intermediary catalytic position in aerobic oxidation, as I interpret it, (page 56).

A very serviceable method of producing the oxyketenes and ketenes is through the phosphoric and sulphuric acid derivatives of fructose, glucose, ether and acetaldehyde, by which the active bodies are trapped as polymers and then resolved to monomers by destructive distillation and by dilution as described in my patented process. I have used this method since 1920. It proves serviceable to my students.

It is rather interesting to compare the production of curative agents in this way with the production of the most vicious pathogenic agents, and also a possible means of the production of the viruses. They form best during dry weather under influence of the August and September sun when dehydration and peroxidation of unsaturated groups by ultra-violet light is favored, and this in turn favors a polymerization of the unsaturated residues. Quinone production, and fluorescence gives such bodies the power to carry chain reactions that we have described to perpetuate any neces-

sary reaction for their existence when present in a cell that liberates exothermic energy. Thus they practically propagate and interfere with normal function. The rapid recoveries we have produced in infantile paralysis, shingles, and other virus infections by employing the diluted polymers and monomers of our Ketenones seems very corroborative to this conception. (34).

The objective in the synthesis of these bodies therefore is to secure free valency of the highest activity in molecules that are as like as possible to those engaged in aerobic glycolysis, as I have interpreted the process to be. They are the fully unsaturated ketenes and oxyketenes, and the hydroxy-ketones from which these are derivable, and also other possessors of the carbonyl group in highly active state, such as formaldehyde, formic acid, glycolaldehyde, glyoxal, glyoxylic acid, glyceric aldehyde, glyceric acid, glyoxyl-carboxylic aldehydoxy-carboxylic and hydroxyketo-carboxylic acids.

The carbonyl group when flanked by an acetylene radical, as in propargylic aldehyde exerts tremendous but not always controllable catalytic powers. It has however eradicated the worst Vincent's infection, Noma and spirochetal infection for me. On the other hand, carbonyl flanked by amino groups are quite inactive, as in the amino acids,—a provision which protects proteins from catastrophe. Therefore in the production of acquired immunity general proteolysis and desamidation may go on extensively to satisfy a local carbonyl deficiency, caused and perpetuated by a local polymerization or other inactivating catalysis. Acquired immunity is therefore a clumsy application of natural immunity principles.

THEORY OF CATALYTIC ACTIVITY OF THE KETENONES

In the case of the peroxide of formaldehyde (which may be viewed as a half 'Ketene') in the presence of water, the instability is so great that decomposition is about complete within from two to six hours. Attendant conditions determine the rate and the direction of the change and how much tautomeric change to formic acid goes on. It is during this decomposition that the hydrogen atoms are oxidized to water and the carbonyl group is liberated, two such groups uniting to form glyoxylide transiently before they join oxygen to form carbon dioxide. It is an auto-oxidation mechanism. In the decomposition, a migration of hydrogen electrons to oxygen takes place and then a union of oxygen with unsaturated carbon atoms follows. The union of Glyoxylide or malonide with oxygen and its decomposition to carbon dioxide involves two migrations of carbon electrons, one from inside the molecule to the oxygen atoms, and the other within the molecule as the valences split between the oxygen atoms added and join the carbon atoms to which the oxygen atoms are already joined. Both types of electronic migrations have their catalytic values. Very few molecules need be changed to supply the high dilutions used.

The efficiency of activation of the unsaturated groups of the fluorescent substance to unite with oxygen here encountered may be compared with the auto-oxidation of benzaldehyde, where first a peracid, benzoyl hydrogen peroxide is formed, (A) which reacts with further

benzaldehyde to form benzoic acid (B). Baekstroem found that both reactions are sensitive to light, the quantum sensitivity of (A) being of the order of 10^4 , while (B) was much smaller a yield of 17 molecules per quantum (32). Thus the reaction between benzaldehyde and oxygen is highly efficient in causing the activation of fresh aldehyde molecules to react with oxygen. The mechanism is, of course, not fully understood even though in the case of comparatively stable substances here cited the peracid was isolated as an intermediary in the process. Still the ultimate activity is a facilitation of the migration of electrons to oxygen from a system of atoms in a large number of molecules by the act having just taken place or just going on in one molecule, so the medium of the intermolecular spaces must play a part. This medium must therefore convey a sort of resonated radiation between similarly constructed atom groups, which induces electronic migrations in progress in one group to take place in others of similar structure. The phenomenon is exemplified also by experimental mitogenetic radiations and the greater rate of epithelialization of proximate points of a healing wound.

To demonstrate the direct annulment of carcinogenic activity of the highest order, mice were painted with benzene solutions of benzopyrene in concentrations of one to two hundred three times a week for a period of weeks. At chosen periods a dose of one of the peroxides studied or of a crudely prepared solution of glyoxylide was given subcutaneously or intraperitoneally, once in some instances and oftener in others. By comparing the incidence of tumors and cancers in the controls and in the treated animals, an idea of their efficacies is obtained. The peroxide of diformaldehyde shows

splendid activity. The peroxide of formic acid shows less efficiency. The peroxide of oxalic acid in unreported experiments showed no protection, while the peroxide of formaldehyde showed repeatable recoveries from well established cancer as well as prophylaxis. When sufficient time has passed to demonstrate the permanence of recovery these observations will be published. The first observation was made together with Professor Maisin (31) and others were done by Professor Maisin and members of his staff (32) (33).

Protective Action of Diformaldehyde Peroxide

The mice received applications of benzene solution; 1/200 benzopyrene three times each week. The peroxide was injected, 1cc. solution 1/20,000, on the 35th and 65th days.

Groups	Mice at start	Mice surviv- ing to first To cancer	147th day	Day of observa- tion	Relative percent		Absolute percent	
					Tu- mors	Can- cers	Tu- mors	Can- cers
CONTROLS								
1	40	28	21	147th day	53	48	55	48
INJECTED								
2	50	40	27	147th day	4	—	5	2.5

Peroxide of Diformaldehyde

1/20th of a mgm as one dose was given at the end of the first month of benzopyrene application.

Groups	Mice surviving to first cancer	To	Percentage absolute of cancer
Controls	28	120th day	18
		210th day	57
Injected	40	120th day	5
		210th day	7.5

1/10 mgm of the peroxide of diformaldehyde was given as one dose intraperitoneally before the first benzopyrene application.

Controls	78	120th day	30
Injected	75	120th day	10

Mice receiving three drops a week for 6 to 7 weeks of a benzene solution of benzopyrene, of a strength of one to two hundred. For treatment each animal received one dose of $\frac{1}{2}$ cc. of a 1/5000 solution of the peroxide of formic acid.

Groups	Mice surviving to first cancer	To	Percentage absolute of cancer
Controls	68	120th day	45
		210th day	69
Injected	52	120th day	23
		210th day	31

For treatment each mouse received 1/10 mgm as one dose of diformaldehyde peroxide every 14 days after the first application of benzopyrene.

Controls	78	120th day	30
Injected	30	120th day	9

Unsaturated Substances

All mice received twenty applications of a benzene solution of benzopyrene 1/200 three times a week for twenty doses, and then one dose of an alkaline solu-

tion of 0.10 mgm of a fraction of the distillate obtained by the action of strong sulphuric acid upon ethyl ether. This distillate crudely contains, among other things, the sulphurous acid compounds of the diketal, glyoxylide, and related bodies.

EXPERIMENT A

		<i>Controls</i>			<i>Injected</i>		
		Number of mice alive	Percent of tumors	Percent of cancer	Number of mice alive	Percent of tumors	Percent of cancer
Day	60	75	36	1	62	10	0
Day	80	72	50	8	61	30	1.5
Day	100	71	65	16	60	38	4
Day	120	66	67	22	56	38	10

EXPERIMENT B

Day 60	60	71	28	0	75	22	0
Day 70	70	70	40	5	69	27	1

Thus the injected animals demonstrate destruction of the allergenic activity of benzopyrene; both by the unsaturated diketones which may become peroxides within, as well as outside the body, and by the peroxides of substances which in the body may liberate free carbonyl groups to form the unsaturated diketone and also catalyze the peroxidation of formaldehyde. So, in a laboratory way we here hint at their therapeutic value which we have proven nearly twenty years ago by the full cure of human beings suffering with far advanced fully diagnosed cancer; cases that were too far advanced for operation, or were operated by experts with widespread recurrence and extension of the disease resulting.

STANDARDIZATION OF KETENONE SOLUTIONS

In keeping with the fact that photochemic catalysts possess greatest efficiency at an optimum dilution, the standardization of each dose is important. Several methods of estimating activity are available; namely, the direct method of determining the increase in the rate of tissue oxidation secured in living tissues *in vitro*, and clinically the rate of improvement in the dispersion of the blood and tissue colloids dependant upon the removal of toxicity. The former method is carried out in the Warburg chamber in its original or better, an especially adapted form. A glyoxylide solution thus found to increase the rate of oxidation of living tissues between twenty-five and thirty-five per cent in two hours is generally satisfactorily effective clinically as well.

To estimate its efficacy as a direct detoxicant, the rate of fall of blood pressure in hyperpiesis and the rate of return of the basal metabolism rate toward normal from a high or low rate are interesting tests. A fall of fifteen points from hypertension in a half hour indicates an efficient solution. The drop in the white cell count, and the rate of disappearance of an angioneurotic oedema may be used as satisfactory criteria, also. Solutions of a dilution of one to 10^{-10} or even of one to 10^{-30} are found to be actively efficient. These findings have been confirmed by Maisin. However, biological means of standardization are not as satisfactory as accurate dilution of a definite weight of material. The spectrographic qualities and clinical progress secured are the only practical tests we can recommend.

THE RECOVERY PROCESS

The discussion of the recovery course of a large variety of disease expressions according to the same reaction schedule would ordinarily seem strange. Yet the removal of the fundamental basis of allergy and lost immunity should reveal a mechanism of health restoration differing from that based only upon the removal of secondary causes which characterize the specific condition at hand. Within physiological limits any and every disease that could engraft itself upon lost natural general immunity, no matter when acquired, or which of its expressions remain, could rightly be expected to be corrected, if the supportive basis is truly removed. The recovery process should therefore extend back to include the correction of changes remaining from early infection, hereditary injury to the germ plasma, and failures in proper development (22). This has been realized in many instances, not only in the involution of scars that have walled off infection for many years, but also in the restoration of the development of glandular systems as the thyroid and pituitary whose development had been suppressed for a number of years, the restoration to normal of backward children, and sometimes of idiots, and in the descent of testicles, with the recovery from feminism.

The catalysis of oxidation, being basically involved in all normal procedures, exhibits in its reinstatement several very fundamental phenomena, among them the unit of biological time concerned with natural immu-

nity. This feature is resident in two distinct motions, that of the activated electrons of the oxidation chain carrier, and that of the charged particles of the colloidal make-up of the tissues. Both are electric phenomena involving time as a function of space, and since colloidal dispersion depends in the living body upon the activation of oxygen electrons, through the carrier of the oxidation chain, the time unit of the periods of expanded and contracted colloidal dispersion is best observed by contrast during periods both in pathogenesis and during recovery while the oxidation mechanism is still weak. Regardless of the source, so long as the glyoxylide malonide or other catalyst used are energetically active, the recovery process is the same in its cyclic characteristics.

The history of the individual himself, both with respect to the pre-growth toxic state, its psoriasis, neuritis, gastric ulcer, neurosis or what not, and with respect to the mode of development of the malignancy, its periodicity, and its relation to the pre-growth changes will tell much that is useful in the conduct of treatment. Two factors appear in the periodicity. They are environmental and essential. The latter is a genetic affair that is well illustrated in the case of a two and a half year old girl with malignant gliomata of both eyes that had become well metastasized to the lungs and other organs. This child demonstrated mounting aggravations each day of the last quarter of the moon. This was the mother's usual menstrual period. With the next change of the moon, the subjective symptoms improved somewhat, but the progress of the growths made during the bad period would remain stationary until the next last quarter, when another advance in the disease was made. This

change was sharp and invariable whether the mother menstruated then or not. I do not consider this characteristic an environmental affair, well recognizing the fact that light reflected from large surfaces like the moon and the ocean is circularly polarized and can affect photochemic responsiveness. The rhythmicity is probably a part of the larger order of things which takes in the moon changes as one of the concomitants.

However, environmental affairs have their significance; and diet, elimination, toxic exposure, as to terpenes, anaesthetics, narcotics, fatigue, and the like, may set up variations of irregular rhythm. The victim of cancer is a poor oxidizer and susceptible to any form of allergy. In some, the neuroses that Freud bases upon sex behaviors are quite prominent as they are also in tubercular patients. We regard such departures which might be aggravated rhythmically with moon changes as essentially allergic phenomena in which the impulse generative fibrillæ of a certain group of neurones associated in some sex concept have adsorbed the allergenic agent which forces the passage of impulses through the neurone circuits of the group. Though such impulses may be sent out in some instances quite continuously, they may not be able to jump the synapses except under the rhythmic help of cyclic events as accompany the moon changes or various environmental influences, diet, toxins, suggestions, etc. We also regard all insane manifestations as similarly caused.

It is important to study the patient's daily habits and to choose the time of giving the injection of the particular oxidation catalyst chosen at a time when the aggravation first shows up. A close study of the history will reveal the most favorable time.

In the case of the baby with glioma here mentioned we could not wait until the beginning of the last quarter of the moon to institute treatment because she was so far gone that she would not live that long and her suffering was too intense; so the treatment was given at once, two days after the end of the last quarter. Reactions were quite strong, therefore, with fever of one hundred and one and over for about seven days when improvement set in and progressed splendidly. On the other hand, had the treatment been given at the time of beginning strongly increasing aggravation, a rapid subsidence of the aggravation would be expected. Never the less the oxidation catalysts employed abolished the essential rhythmicity since throughout the last quarter of the moon that followed, only improvement was observed.

It is true that the incubation period of cancer may be very long and the infection may attack the parent, producing cancer in the child and the grandchildren, in a very peculiar type of transmission, as occurs regularly in malignant glioma of the eye demonstrating its action through the genes. Moreover the infectious origin of allergenic toxins is neither impossible nor devoid of other examples. The tubercle bacillus produces such a toxin and the allergy may be expressed not only in an increased susceptibility to the products of the tubercle bacillus itself by an allergic necrosis in skin, lung, and joint tissue, but there may be terrific and prolonged allergic migraine, multiple arthritis of advanced degree, and even a coronary thrombosis as well, occurring in the same patient. Recovery takes place from all four conditions on the one treatment and the orderly disappearance of the various allergic changes follows the clearing of the system

from tubercular lesions, scars, and their debris, and the re-establishment of healthy lung tissue to take their places. Even in these secondary allergies an essential rhythm belonging to the original disease may show through.

The recovery process is cyclic, (23) the shortest time unit being possibly twelve hours, although the shortest unit easily observable is three and a half days or eighty-four hours. These units are doubled and tripled and further multiplied into cycles of three, six, nine, twelve, and twenty-four week periods or longer periods, all of which are multiples of three. Each cycle is comprised of a positive and a negative phase. During the negative phase there may be chills and fever in cancer or one of the chronic infections as tuberculosis, leprosy, or syphilis. The fever is not the result of colloidal lysis taking place in normal tissues, as occurs in infection or after tissue injury, but rather results from the burning of accumulated unoxidized fatty and waste material and the digestion of proteins of the neoplasm. Hence, the reactions may be accompanied by, or are soon followed by, an improvement in well being. Such reaction periods may last a few minutes or several hours or a few days. During the positive phase, improvement in general health, healing, and reconstruction of the local lesions to normal is observed. In this healing, scar tissue is not permanently produced, but rather a reconstruction of the organ by normal tissue elements takes place where this is possible. Therefore normal function is restored. Even when the treatment is given in cases with old scars formed many years previously to wall off infection, we expect the scar to disappear as the infection it encapsulates clears away consequent to the develop-

ment of immunity by the Ketenones. Such scars are not present to fill in space, but rather serve as barriers to the infection they carry through these years, and immunity to the infection disposes of their usefulness.

Biopsies taken from malignancy lesions at different phases of the reaction cycles display the local recovery mechanism. First a coagulation necrosis takes place in the malignant cells, the younger cells undergoing the changes the earliest, and the older cells following along more slowly. A calcification of the cell plasma plus nucleolysis sets in early; and soon small buds of vascular tissue preceded by a zone of liquefaction in the coagulated cells are seen to penetrate and absorb the coagulated material until the tissue becomes entirely absorbed and organized with vascular tissue. The process resembles the removal of a blood clot. Normal tissue elements soon appear and a reconstruction of the destroyed tissue is accomplished. Large areas of visceral walls are thus restored. Rectovaginal fistulae two inches in diameter or larger have many times healed to complete normalcy in this way so that no trace of injury can be found. Bone areas four inches in diameter completely destroyed have been fully replaced. The shafts of the long bones and the bodies of the vertebrae, the illia, and other bones have many times been repaired with a bone substance somewhat denser than normal bone, (24), (25). First the soft bony structures are reformed with restoration of the normal shape and then calcification and hardening takes place, so that distortion is overcome. In the healing of a fistula, left by absorbing the neoplasm, healing about the edge with epithelium is accomplished and the tissue elements extend inward toward the center of the opening, the edge always still covered by epithelium



Fig. 1.—Microphotograph (magnification 150 times) of squamous cell carcinoma of skin before treatment.

till only a pin point hole remains which finally closes. No supportive bridge is therefore required.

The criteria as to favourable progress, are not only the occurrence of reactions and greater well being with absorption and healing of the lesions, but also the blood changes indicated by the differential vanadium reactions worked out by Bendien and E. Cronin Lowe, (8) (9) the criteria as to improved colloidal dispersion described by MacDonagh, (10) and by improvement shown by the blood crenation test. The latter has a

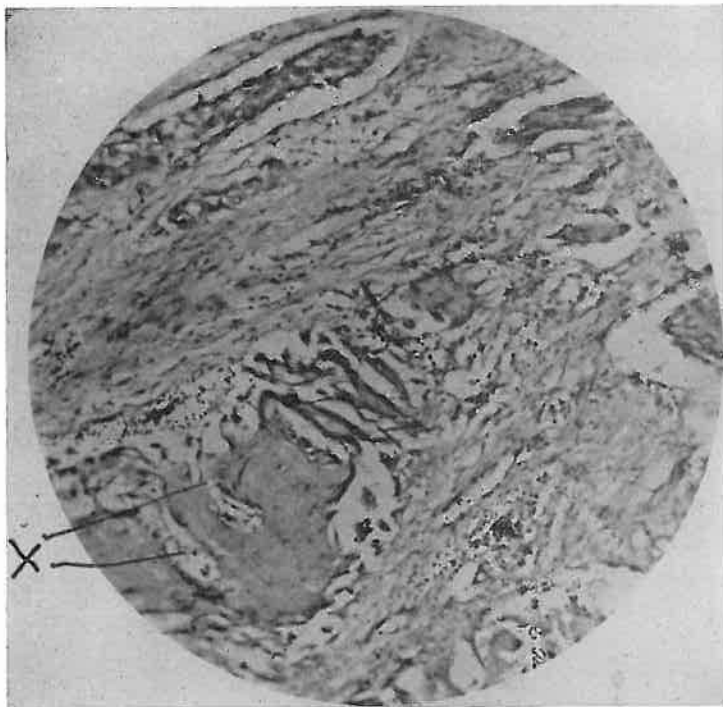


Fig. 2.—Microphotograph taken from same growth as Figure 1 several weeks after patient received the glyoxylide injection. Here the cancer cells are nearly completely digested and swollen up to form gelatinous agglomerates. The small blood vessels are seen growing up into and about these gelatinous groups. As fast as the digestion of the cancer debris progresses, the products are absorbed by the blood vessels and carried away by the circulating blood and used for the general nutrition of the body. Finally, the whole cancer mass becomes replaced by small blood vessels as the debris is digested and absorbed.

double significance, since in malignancy the number of the red cells that do not crenate in a one per. cent salt solution is proportionate to the injury to the oxygen carrying power of the blood and also to the injury



Fig. 3.—Same as Figure 2.

to the reticulo-endothelial system. As the cells become able to crenate in greater numbers, the improvement in both respects and the lessening of the toxic factor becomes evident. Moreover, in patients exhibiting a low crenation number and marked anemia, improvement of the oxygen supply by subcutaneous injection of oxygen gas may occasionally prove helpful.

There are a number of interfering factors which may interrupt the recovery process for a time or permanently; and inasmuch as the ketenones are photochemic in their action, electromagnetic waves of correct fre-

quency are important in this respect. Geologic environmental features that cannot be definitely identified are thought to probably belong to this group. Improper diet and fatigue are factors which may interfere also.

It is well known that tumor cells respond, not only to chemical stimuli but to physical stimuli as well. Many surgeons lack accurate tactile sense and employ such excessive pressure in making physical examinations that they actually stimulate cell activity which in malignant neoplasms can bring about but one response, namely that of cell division. In making examinations the pressure used should not exceed that to which the cells are accustomed, and this pressure is equal to the blood pressure only. Whenever an examination has caused pain during the examination or even worse the next day, that examination has done harm for it has stimulated the growth by a mechanism that is physical and against which no anti-allergic measure can have any effect. I have had clinical assistants who persistently made crude rough examinations in spite of advice to do otherwise. Their recovery percentages were poor indeed. It is therefore better to sacrifice data as to exact anatomical extensions of a growth to the better cause of giving the patient the fullest opportunity to recover.

The deeper the disease, and the more chronic its course, the longer the time required for recovery, or even for a reaction to the treatment. Many a time in my early experience have I sent a cancer patient home telling her that since I observed no response to one dose in the first few months that the treatment did not fit her case. Many a time I was wrong in so doing for after a few more months reaction took place. Recovery in the course of a year or two also followed. The best reactions may not come till the seventy-second week after treatment. The time factor is just as important as every other factor.

THE CARE OF THE PATIENT

To fully appreciate the objectives of this treatment method it is well to recall the various natural mechanisms for combating injury to the normal body chemistry. With increasing knowledge of colloidal chemistry we are inclined to look upon the various antitoxins, agglutinins, lysins, etc., of immunology as states of dispersion of the tissue colloids rather than as new substances generated within the body (10) (14) (15). MacDonagh has discussed these matters in detail and has emphasized the part played by the glands of internal secretion in the maintenance of the colloidal dispersion favorable to good health and resistance to disease. Fundamental to this however both in the development and function of these glands, stands the catalysis of oxidation just as it is basic to the development and activity of each cell's functional units.

My work on the parathyroid glands, (18) (26) (27), demonstrated that an endocrine gland may make a business of actually destroying a toxin of specific chemical structure, the guanidine bases for instance. It appears that this destruction of guanidine is accomplished by both building this substance up into a useful substance, creating phosphoric acid, or guanine, and by oxidizing the excess to urea. So the parathyroid glands preserve the colloidal dispersion that keeps the cations like calcium adsorbed into the living colloids, and thus prevents their loss through ionization and diffusion. It is at the expense of the oxidation mechanism that the energy needed for charg-

ing the particles in the sense of MacDonagh and for the synthetic or oxidation work necessary to the disposal of toxins is gained. Likewise, the pancreas works at the expense of the oxidation mechanism to lower the surface tension of the tissue colloids so their lysed particles may adsorb each other till their surface area is reduced to a point where the energy per unit surface has increased to normal and a substitute for normal dispersion with correct adsorption of sugar and electrolytes has been attained. The return of function of incapacitated endocrine glands, the thyroid, the pituitary and the sex glands, as well as the restoration of their development after it has been intercepted even for a number of years, illustrates the fundamental position of restored oxidation catalysis in the defense mechanism. Case histories are given to exemplify these facts.

Since malignancy rests upon total anaplasia or a potential anaplasia expressed in hypoplasia, the restoration of normal cell development with its functional elements is a physiological measure of combating cell perversion. But this, too, depends upon an oxidation catalysis that destroys the offending traumatizing allergenic anaplasia producing toxin. After the Ketenone treatment is instituted, the restoration of the normal colloidal dispersion consequent to the restored oxidation mechanism should be permitted to follow without aid of endocrine or medicinal means. All chemotherapy aimed toward helping out may prove disappointing by blocking the normal restoration procedure. Time should be allowed for the natural reconstruction and return of function of any deficient organ; and proper food, rest, and elimination is all that need be required. There are several ways in which

interference takes place, but the photochemic means of destroying the oxidation mechanism are most dangerous. Anesthetics and narcotics destroy the colloidal dispersion that provides the correct surfaces for mediating the oxidation reactions. So profound may injury from anesthesia be, that where a commanding infection is present as in pneumonia, or septicemia, anesthesia may spell death. It is much more difficult to restore immunity under such circumstances if the general anesthetic were used during the recovery from infection in response to the glyoxylide. The routed dispersion of the colloids and the destruction of dehydrogenases may not be correctable in time to save life by further doses of this catalyst.

Substances that photochemically quench the catalytic activity before it gets well started should be eliminated from the regime. The chief offenders are substances of similar structure to the glyoxylide and sometimes a dose of the catalyst itself given at a wrong phase of a recovery cycle. Such substances absorb in the same spectrum ranges and act by resonance induction as described by J. Perrin, (13). In this connection it must be remembered that if a recovery process has been instituted by the glyoxylide as a member of one equilibrium system, repetition of the dose with the glyoxylide from a different source may annul the activity of the first dose because different systems do not possess identical intensity of electronic activity. Substances which quench fluorescence cannot contribute helpfully and must be avoided even though without the glyoxylide they may prove beneficial. Such substances are active in proportion to the ease of displacement of the electrons of the peripheral shell of the anion, in the following order, (28), I' CNS', BR', CL', OX',

AC', SO₄', NO₃', FL'. It is in this way that the Calcaria Fluorica of homeopathy occasionally proved useful in cancer, and would detrimentally quench some of the energy of the glyoxylide, if given to a treated patient. It is best to avoid all medication, therefore, unless experience has proven its harmlessness in similar cases under this treatment.

The sedimentation rate of the red blood cells is generally a fair index to the degree of toxicity of an individual, the degree of entropy of his colloids and the loss of vital energy from the colloid surfaces. Normally, the drop is only a few mms. for a healthy individual, but this small amount varies with the individual. In cancer, tuberculosis, and the allergies, the drop is great or moderate according to the degree of illness presented. After successful activity of the Ketenones the improvement in the sedimentation rate follows the clinical improvement closely, and the test is valuable in estimating improvement. Generally during the fourth week it has improved far towards normal, indicating the decrease in the amount or effect still remaining from the causative toxin. What we have said about photochemic extinction of the action of fluorescent toxic substances can be nicely exemplified by a diagnostic study of my assistant, Dr. Gerrit J. Warnshuis. He observed that if a drop of a dilute solution of tuberculin were mixed with the citrated blood employed for the sedimentation test, the rate of sedimentation was diminished both in cancer, tuberculosis, and in the allergies. The rate is not changed thus in the normal blood except in some apparently healthy people whom we are watching with the suspicion that they are very early or pre-allergic cases that will later on show physical signs of disease that

can be detected. In these persons the ketenones bring about normalcy, in that the decrease produced by the tuberculin in the sedimentation rate no longer occurs, and also improve the health subjectively. Possibly an important prophylaxis is thus accomplished, and demonstrated. In the truly normal blood an increase in the sedimentation rate occurs, however, on addition of tuberculin.

Where disease exists, the addition of the tuberculin causes a lessening of the sedimentation of from a third to a half, roughly speaking. Ordinarily one would think that increasing the amount of poison would increase the sedimentation rate. But when we view the matter from the standpoint of photochemistry we can understand why it must be otherwise, for the added tuberculin absorbs energy in the same ranges as the toxin that is basic to cancer, tuberculosis, leprosy, and the allergies. Thus the radiation of electronic activity of the causative toxin is absorbed by the tuberculin and the injury to the colloidal dispersion is lessened proportionately. When all toxin is disposed of by the Ketenones, tuberculin addition to the blood, thus become normal, or to an otherwise normal blood, increases the rate of sedimentation. Thus we observe the toxic effect of the tuberculin only, on the colloids, and a diagnosis of recovery from this standpoint is made possible. We have found agar to behave in much the same way. It is interesting to note that the poison of malaria which is able to absorb the energy of the syphilis poison, is rapidly destroyed by our oxidation catalysts. Thus patients with regularly recurring attacks of malaria cease to have attacks after the Ketenones are used. The basic toxic structure

of the diseases concerned are thus similar, and yield to the same chemical attack.

Diet and Technical Precautions

Vegetable, fruit, and whole grain cereal diet, avoiding coffee, tea, chocolate, alcohol, spices, tobacco and the terpene derivatives of tropical fruits and their skins; the use of bowel lavage with salt water when necessary, fresh pure air, pure water, plenty of rest, and reasonable exercise constitute the regimen. One dose given intramuscularly is the favored practice. The treatment need not be repeated in some cases, but two or three injections at fourteen day intervals may or may not be required, depending upon the response of reaction or improvement. Three and a half or seven day intervals, or a three or twenty-fourth week interval may be the correct timing of repeated doses. Rarely are more than three needed in any case that is able to recover. The dose should never be repeated if improvement is in progress, especially at the seventh, fourteenth, or twenty-eighth weeks. And it is always best to let progress continue as long as possible, even for ninety-six weeks, or to complete recovery without repeating the dose. For open wounds cornstarch dressings are preferred. An accurate chart of the reaction features should be kept to establish the time relations of the recovery process of each patient.

Five grains of potassium iodine for a few days may be required to overcome colloid hydration or iodine deficiency that delay recovery.

A dilute solution of a highly unstable substance may easily be rendered inactive by the slightest contamination. Therefore in the preparation of the Ketenone the

most scrupulous cleanliness is required not only with regard to apparatus and materials, but even the air must be as pure. Air of ordinary chemical laboratories and the air of industrial cities is prohibitive of best success. In giving the injection care must be taken to clean the skin and remove all traces of the cleanser and thoroughly dry it before the injection is given, and it is reasonable to request after all of the fastidious care spent in avoiding even the most minute traces of contaminations in the preparation of the material that it should be drawn from the ampoule into the syringe only in a pure atmosphere. After the injection is made the selection of foods and medication must be done logically.

The most certain means of wiping out the recovery mechanism, let me repeat, is an anesthetic, ether being the most effective. Narcotics of all types are active in similar fashion in varying degrees and alcohol is not innocent. Fortunately pain is relieved in many instances very early after the glyoxylide is used and narcotics can be discontinued. Whenever possible other means of controlling pain than drugs should be used. Where there is colloid lysis because of infection, the action of anesthesia may so profoundly injure colloid dispersion that a come-back is made impossible or nearly so, and the benefit secured by the Ketenones is completely wiped out. Therefore if a surgical procedure is called for and cannot be delayed, it should be done first and the Ketenones should be given within a few days to help overcome the injury caused by the anesthetic as quickly as possible. It is well to repeat the dose in eighty-four hours or in a week in such instances.

Important as the colloidal state of living matter

is known to be both to metabolic processes and to immunity, the exact mechanism by which the structural surfaces function is not fully known. That the electric charges carried are important is quite evident and likewise is appropriate surface tension necessary to favor adsorption of the crystalloids whereby their concentration in ionized diffusible form is regulated. It may be argued that the reactive materials are thus concentrated in the colloidal surfaces and hence are more ready to enter into chemical reaction with each other. But I prefer to think that some substances, at least, by being adsorbed into the colloidal surfaces are reduced in concentration just at the surfaces to the point where the critical temperatures of their reactions are lowered to the body temperature, and hence can be carried on in optimum fashion under physiological condition.

The effects of soluble aluminum compounds, of bismuth, hydrogen sulphide, and the amines of putrefaction formed in the colon and in anærobic foci of infection and the effects of tannin on colloidal state have not been studied enough. Yet we know that these substances inactivate catalase and peroxidase of the tissue cells and hence they are primary factors in the injury of the oxidation mechanism, in that they permit the existence of stable peroxides that favor polymerization of the substances that should peroxidize and burn rapidly; and by injuring the protective oxidation mechanism of the intestinal mucosa they favor the entrance of disease germs and poisons into the tissues. Thus a faulty diet is the earliest factor, like the exhaustion of fatigue, in the causation of disease. These matters must be considered seriously in the treatment of disease and we do not neglect them in our regime.

CASE HISTORIES

ALLERGY OF THE PLASTIC SYSTEM

To illustrate a few of the practical features of the treatment several case histories are submitted. Some of the first cases of malignancy treated in 1919 are still alive and well. Those that have died in the meantime (years after the last glyoxylide treatment) did not die of cancer. Autopsies demonstrated the cause of death to be injury through skull fracture, senility, heart failure, or pneumonia. In the meantime many physicians have used the treatment with a recovery percentage ranging from twenty to over eighty per cent in advanced malignancy cases. The recovery percentage depends upon the recovery advantage the patient presents, the reasonableness of his co-operation, and the good judgment used by the physician, as well as upon the efficacy of the remedy itself.

The usual allergies and infections respond more rapidly than malignancy. Severe cases of shingles are often relieved in three hours and recover in a few days. Although psoriasis may recover completely in fourteen weeks, it may require a year or longer. So long as recovery is in progress from one dose it is not repeated and may prove sufficient. On the cases here reported in accordance with our general rule, no therapeutic measure was employed along with the glyoxylide or malonide. Except as otherwise stated the glyoxylide was prepared from the sulphonic acid derivatives of ethyl ether, glucosé and fructose phosphoric acid derivatives.

CANCER OF THE BREAST

Mrs. M.—Age 36.

Family History—Father's death may have been from cancer. No tuberculosis in family.

Past Illnesses—Persistent tonsilitis. Tonsils removed twice, headaches, and dizzy spells.

Present Illness—Started seven years ago, 1929, as lumps in both breasts. The right breast gradually cleared up, but the left breast increased in size through increase in the tumor. Examination by a cancer surgeon of wide reputation was made on January 4, 1935. It was so far advanced, infiltrated, and metastasized that he gave a diagnosis with full certainty from the gross pathology and refused to attempt any help because it was too far advanced. She then went to an escharotic institution where the attempt to remove it was made. Only an incomplete destruction was accomplished and it soon returned. A second attempt with escharotics was made in July, but only added to an aggravated recurrence and spread over the chest wall and throughout the axilla and above the clavicle. There was backache indicative of spinal metastases.

Two malonide treatments were given three days apart and recovery was completed before June, 1937, when examination revealed full absorption of all growths and full healing with also a good return of general health. She remains well.

In this case a low grade malignancy was aggravated by chemical stimulation of the escharotic. The recovery response was rapid in keeping with the general rule that the recovery rate is proportional to the rate of growth.

CANCER OF UTERUS

Mrs. T.—Age 31. Squamous cell carcinoma of cervix uteri. Biopsy confirmed by three different pathologists. Report reads: "Sections show an atypical proliferation of squamous epithelial cells which have markedly infiltrated the underlying tissues. Diagnosis—Squamous cell carcinoma (Epithelioma)." Surgically inoperable, invading body of uterus and adnexia. Severe hemorrhages and pain, cachexia, no children, one miscarriage. Treated with two doses of glyoxylide solution, one cc each, two weeks apart, August, 1923. Recovery followed with complete restoration of uterus in one year. Four healthy children born since. Perfect health remains.

TOXIC GOITRE AND CANCER OF THE STOMACH

Mrs. W.—Age 58. History taken, September 25, 1927.

Family History.—No cancer recognized in ancestry. Husband died of Cancer eight years previously, daughter, age 28, had brain tumor cured by glyoxylide. Her home, in the goitre belt of Ohio.

Present Illness.—Started several years previously as steadily increasing nervousness, circulatory weakness perspiring, loose bowels; and tremor. Radiographs showed enlargement of the heart, in 1927. Exophthalmus became quite noticeable and increased, the skin bronzed and gastric symptoms set in. Loss of weight from 150 pounds to 108 took place while the feet and legs became œdematous, and the head and neck veins engorged with blood, showing obstruction to the venous return to the heart, percussion showed marked in-



Mrs. T. and her three children which were born after recovery from extensive cancer of the uterus. Diagnosis made by physical examination, the history of the case, and confirmed by microscopic examination of specimen removed from the growth. Specimen was reviewed by other pathologists to confirm correctness of original diagnosis. Treated 15 years ago, now has four children and is in perfect health.

crease in the mediastinal density. On her visit to my clinic her chief complaint was severe pain in the right lower ribs and epigastrium. Examination revealed a large bulging mass somewhat lobulated bulging from the epigastrium and the right hypocondrium. There was also a walnut size mass in the left supraclavicular space. Stools showed occult blood, there was vomiting and great weakness.

Treatment.—One cc. of glyoxylide was given September 28, 1929. Recovery was steady with regular three week reaction periods showing some chills and fever. Complete recovery was established by her sixtieth week. The photographs show recovery from the exophthalmus. The first one was taken before treatment, and the second on June 18, 1933. Her health is perfect still she reports.

CANCER OF TESTIS

Mr. T.—Age 38. Medullary carcinoma of testis, recurrent after two operative attempts at removal. Biopsies done at these operations confirmed diagnosis each time. The last biopsy report reads: "Carcinoma probably secondary to previous carcinoma of testis as the cells were histologically similar." Recurrences involved scrotum, abdominal wall and structures of lower abdomen. Patient weak, cachetic. Treated once, June 10, 1925. Recovery complete in six months and has remained well ever since. Is very hardy and strong.

CANCER OF LARYNX

Mr. M.—Age 58. Treated once, November, 1928. Diagnosis confirmed microscopically by two different



Mrs. W. before treatment showing typical exophthalmus from toxic goitre reported in this series.



Mrs. W. showing recovery after the antitoxin.

pathologists. "Squamous cell carcinoma of larynx showing many epithelial pearls." Involvement, vocal cords and cervical glands extensively. Voice and breathing impaired. Recovery complete within six months. Remains well. The peroxide of formaldehyde was the source of the glyoxylide in this case.



Mrs. C. with baby born three years after recovery from very advanced cancer of the uterus, adenocarcinoma microscopically. In this case the whole pelvis was solid with the growth and the uterus seemed mostly eroded away. Patient could not walk, cachexia was advanced and she was bedfast. All parts are perfectly reconstructed and she and the baby are perfectly normal.



Mrs. F. and child. Mother had complete diagnosis of cancer and judged far advanced and inoperable 10 years ago, completely cured by one dose of glyoxylide 9 years ago.

CANCER OF STOMACH

Mrs. P.—Age 61. Treated twice, two week intervals, November, 1919. Massive carcinoma of stomach widely infiltrated and metastasized causing complete obstruction of pylorus. Diagnosis confirmed at laparotomy. No biopsy made, or needed. Patient emaciated, bedfast. Two weeks after treatment growth considerably absorbed and pylorus opened up permitting



Mrs. P. and two children born after recovery from generalized melanotic cancer recurrent after two operations and involving liver, stomach, uterus and pelvis generally, causing apparently great destruction of uterus. All have perfect health.

passage of food. Thereafter recovery rapid. Patient remains well to date. Excellent health. Cephaline fraction of heart muscle extract was used as source of glyoxylide in this case. Reported in Medical Record, October, 1920.

CANCER OF STOMACH

Mr. R.—Age 69. Treated once, August, 1926. Medullary carcinoma of stomach. After gastroenter-

ostomy, to relieve pyloric obstruction, the neoplasms spread extensively, completely closing the new opening. Diagnosis confirmed by biopsy. Biopsy report:

"Microscopic Examination: Small alveoli combined with a diffuse growth of atypical proliferating epithelium form the structural picture of this neoplasm. The epithelial cells are generally polydecral or round in shape, with large hyperchromatic nuclei. One portion is necrotic—a superficial ulceration. This may be classified as the diffuse type of gastric carcinoma. I am unable to determine this point exactly as it is necessary to know something of the gross appearance. If there were extensive involvement of the wall, this would be the correct interpretation. If the growth were sharply defined, rounded and ulcerating, it would be placed with the circumscribed types of carcinoma simplex.

"This type is always infiltrating and early invades the lymph nodes with widespread metastases.

"Diagnosis: Carcinoma of the stomach. (Type dependent upon the gross pathological anatomy.)"

Bulging mass fist size when treated August, 1926 with one cc. of glyoxylide solution. Recovery complete in six months. Natural opening at pylorus now functioning, but gastroenterostomy healed shut. Remains well and vigorous at age 80 years.

CANCER OF RECTUM

Mr. M.—Age 44. Terminal case of adenocarcinoma of rectum. Biopsy before surgery and radiation reads: "Polypoid adenocarcinoma. It is of course impossible to state how deeply this is infiltrating or how extensive it is."

Biopsy after failure of these methods reports:

"The specimen represents a fungoid type of growth which is soft in consistency. Two sections are saved.

"The tissue in all parts of the fields examined exhibits an actual diminution of the supporting tissue and an increase of the epithelial structures. The gland epithelium as well as the gland morphology are abnormal, a marked productive change has occurred. The new growth material is distinctly anaplastic and differentiation is not good for rectal tissue. The stroma is infiltrated with small round cells, the tissue resistance is poor and the growth activity is marked.

"Adenocarcinoma of the rectum, *Active*."

When treated with Glyoxylide, October, 1922, patient practically bedfast, cachetic, edematous. Blood picture twenty per cent of normal. Rectovesicular fistula. Feces pass through penis. Considerable bowel obstruction. Putrid drainage, bleeding. Incontinence, massive metastasis in abdomen and liver. Two treatments of glyoxylide at two week interval resulted in complete recovery. In very good health in one year and remains in very good health today.

SARCOMA OF BONE

Mrs. S.—Age 35. Treated June, 1935. Osteosarcoma of right ilium confirmed by biopsy. No attempt at surgical removal. Metastasized generally throughout abdomen and lungs, as large masses. Cachexia extreme, dyspnoea, cyanosis, cardiac exhaustion, bedfast. Recovery required one year. Remains well.

CANCER OF BREAST

Mrs. S.—Age 51. Sister died of cancer of the breast. Present illness started as a tumor under right

arm when seventeen years old. Did not trouble until 1927, when it started to grow and pain her. Radical removal of breast was made in November, 1927. Recurrence about operation incision and in the axilla and above the clavicle was well advanced as numerous growths ranging from pea size over the chest wall to egg size axillary growths when presenting herself in September, 1929. There was also a metastasis in the lower end of the right femur. Treatment, malonide solution was injected in upper arm; and recovery followed steadily and was completed within nine months. Reports at present confirm completeness of recovery.

PRIMARY CANCER OF BRONCHUS

Mr. W.—Age 46. Treated in March, 1931. Diagnosis by bronchoscopy, far advanced dyspnoic emaciated. Unable to walk at time of treatment. Lungs and liver greatly involved. One treatment of Glyoxylide was followed by complete recovery within one year. Perfect health ever since. Doing hard labour.

CANCER OF PROSTATE

Mr. B.—Age 68. Enormous cancer of prostate and urinary bladder with groin and abdominal metastasis. Diagnosis confirmed by biopsy by two different pathologists. Treatment given October, 1927 and June, 1928. Recovery complete within six months after second treatment. Remains well. No more pathology, good strength, normal function, and reconstruction. Potassium salt of glyoxylic acid used as source of Glyoxylide in this case for the first dose. Two cc. of a dilute solution of Ketenes was the second dose.

CANCER OF STOMACH

Mrs. H.—Age 47. Duration two years. Symptoms of vomiting and hemorrhage, rapid growth of tumor to a large hard bulging mass filling the region above umbilicus. Hemoglobin 80 per cent. Jaundice, marked chachexia. Radiograph demonstrates involvement of lesser and greater curvatures from pylorus to cardiac portion. One cc. of solution of Glyoxylide injected subcutaneously in arm October, 1934. Recovery with several reactions at three week periods was completed in a year. Normal in every respect. No pathology at present. Peroxide of formaldehyde was source of Glyoxylide in this case.

CANCER OF PALATE

Mr. J.—Age 60. Cancer of hard and soft palate. Recurrent after removal surgically. Biopsy confirmed squamous cell carcinoma. Nine small growths up to a lima bean in size. Glands under jaw enlarged and infiltrated. One cc. Glyoxylide solution given December 3, 1932 was followed by steady recovery within six months. Remains well.

MALIGNANT GLIOMA OF THE EYE

Baby R. L.—Age three years and six months. First observed by me November 21, 1935. Right eye was removed May, 1935 for rapidly developing glioma.

The removed eye showed the following:

Gross Pathology: Eyeball having a normal external appearance. On section, the posterior chamber is practically filled with a greyish friable tumor mass

which seems to be attached to the region of the nerve head.

Microscopic Pathology: Section of tumor shows rounded dark staining nuclei of cells practically devoid of cytoplasm set in a thin connective tissue stroma having no characteristic arrangement. Marked necrosis is present in some areas and round cell infiltration may be seen in some areas. Section of nerve head shows no tumor tissue.

Pathological Diagnosis: Glioma of retina.

In November, 1935 the other eye was found to be similarly affected. Surgeon advised that its removal would be useless and patient was referred for a dose of Glyoxylide. At this time pains were a prominent feature, eye was red, pupil dilated and apparently paralyzed. Visual field was diminished by one quarter its area, and the neoplasm was visible as a mass about the size of a bean. Malonide was given November 25, 1935 and August 18, 1936. Recovery was completed within a year. During the reactions mild muscle twitchings in the legs took place at the twelfth to the twenty-fourth week period. This we interpret as evidence of reaction in multiple gliomata distributed in parts of the central nervous system. The results are a return to normalcy of the eye in every respect, and a very good condition of her health in general. She goes to school.

FIBROMYOMA OF UTERUS

A most interesting case is that of Mrs. T. who aborted while visiting friends in London. A large fibromyoma could be felt through the abdomen, which observation was confirmed by the family physician. An

eminent surgeon recommended immediate operation, since she had been flowing very freely during her menstruation. Koch Ketenones were given shortly after this. She became pregnant and was delivered of a healthy child two years and four months after treatment. No fibromyoma can now be felt. Her periods are normal and were normal from the time the treatment was given.

The responsiveness of uterine fibroid has always been encouraging, indeed.

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FIBROID OF UTERUS

Mrs. B. M.—Age 39. Colored.

Family History—Does not show cancer or tuberculosis.

Previous Illnesses—No children. Never sick since childhood. Allergic to milk and corn.

Present Illness—During last few years noticed hard lumpy swelling in abdomen. Free flowing for six to eight days at periods, always regular otherwise.

Examination—Reveals lumpy enlargement of uterus by multiple fibroids causing uterus to extend above umbilicus and bulge like six or seven month pregnancy. Cervix not infiltrated. Uterus movable. Compression of bladder causes frequent urination of small quantity. Compression of bowel estimated by examination. Growth rests against sacrum; causes pain and constipation.

Glyoxylide was given January 10, 1930. Recovery took nearly two years from this one dose. The allergy to milk and corn have also left. Uterus now normal and general health very good.

FIBROID OF UTERUS

Mrs. J. C.—Age 47.

Family History—Mother and two sisters operated on for fibroids.

Past Illnesses—Tonsillitis, headaches, and scotomata.

Present Illness—Started to call attention because of flowing between periods in July, 1932. Since December, 1933 has been flowing almost continuously, and the growth that enlarged uterus to the size of a three months' pregnancy, twenty years ago, had now greatly enlarged reaching above the umbilicus and bulging like a six months' pregnancy. There was bowel and bladder compression of marked degree.

Glyoxylide was given April 23, 1934. Recovery took less than two years to be completed, but the abnormal flowing ceased completely within two months, and was nearly normalized after a third week reaction of chills and fever and the passage of much pus and blood per vagina. Her health is splendid.

CANCER OF UTERUS

Mrs. S.—Age 60. Housewife. History taken May 3, 1932.

Diagnosis—Cancer of uterus involving whole abdomen by exploratory laparotomy.

Heredity—Mother died of cancer at age 88.

Past History—Urethral caruncle for last eleven years, very painful and troublesome for last two years. Ulcer of duodenum demonstrated by X-ray four years ago. Large fibroids were removed at time of menopause twenty years ago. Four successive attacks of pneumonia more than five years ago. Weak heart for

last five years, causing blood pressure to fall from 200 to 160 in last year in spite of increasing toxemia. She became short of breath and cyanotic, her feet and ankles swollen with dropsy. Severe hemorrhages from vagina and pain in the back for the last six months. The abdomen was enormously enlarged with cancerous tumefaction.

Examination—My examination revealed a large transverse operative scar and a similar vertical exploratory incision scar. The whole abdomen bulged from the presence of the large masses of cancer within, as is shown by the first photograph taken before treatment May 3, 1932. Thus the stomach, bowel and uterus were all involved and she was suffering hemorrhage because of the malignancy. The large ulcerated urethral caruncle was noted and the vagina found well filled with the malignancy that involved the uterus and abdomen. She was weak, cyanotic, short of breath and the heart was so dilated that one was forced to doubt if she would reach home before her heart failed.

Treatment—Two cc. Ketenes solution, May 3, 1932.

Results—Recovery was comparatively rapid, the cancer masses disappeared, the vaginal bleeding stopped and a return to normal was complete by April 10, 1933, when the second photograph was taken. At this time no pathology could be found, every trace of the growths had disappeared, all the stomach symptoms gave way to perfectly normal function and, although the heart action was not as perfect as in the average healthy person, it had improved so much that we considered her cured. In 1934 she had an attack resembling appendicitis. Her surgeon made an appendectomy and at the same time thoroughly explored the abdomen,



Mrs. S. before treatment. Note the enormous bulging of the cancer masses above the scar of the operation incision.



Mrs. S. showing abdomen returned to normal—note position of scar with reference to rest of abdomen.

and reported to me that no trace of cancer could be found. Photographs on page 123.

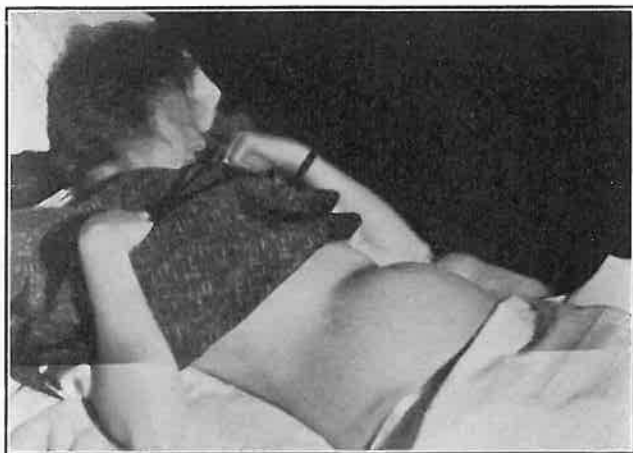
MALIGNANT CHANGE IN MYOFIBROMA OF UTERUS

Miss G.—Age 45. History taken December 2, 1930.

Diagnosis—Malignant change in large fibro-myoma of uterus.

Present Illness—She had suffered with backache for a number of years and three years ago felt the presence of a tumor in the lower abdomen. It grew larger, especially after the menopause two years ago, when with a spurt of speed it began to bulge even above the umbilicus. Glyoxylide was given on December 2, 1930, May 16, 1931, and May 9, 1932.

Results—Recovery was complete before the end of 1932, as the second photograph shows. At that time no more of the mass could be palpated by most thorough examinations. The first few months brought the greatest change in the size of the growth. The material that underwent most rapid digestion and absorption we consider to have been the tissue of malignant character, and the slower portion to leave was no doubt the original fibroid material. After the majority of the growth, the malignant part, had disappeared, she had a return of pre-growth symptoms, iritis and photophobia for a week, that was very troublesome but did not prevent her from attending to her work. Since that time her vision has improved and her hearing is definitely better. She is in perfect health. Photographs are produced on the following page.



Miss G. before treatment. Note the large bulging growth that filled the lower abdomen and compressed its contents.



Miss G. after recovery, every trace of the growth absorbed, and abdomen normal.

CANCER OF URINARY BLADDER

Mr. H. A.—Age 69. Salesman. History taken February 16, 1931.

Diagnosis—By history, exploration and physical and X-ray findings.

Pre-growth Symptoms—Psoriasis on both elbows for many years and neuritis for last five years.

Past Illnesses—No serious sickness except a Neisserian infection many years ago.

Present Illness—The trouble started as difficulty in passing urine, pain and frequency every half hour when on his feet and almost as bad at night. Cystoscopy at the Cleveland Clinic revealed a well-developed cancer of the bladder and calculi embedded in the growth. X-ray examinations showed that the pelvic bones were involved. At least one-half of the ilium and ischium were involved in a mass that could be palpated through the abdominal wall to be as large as three fists. They gave him an X-ray treatment and he grew progressively worse.

Physical Examination—He presented himself at my clinic, suffering twice the frequency of attempt to pass the urine and the pain was worse. The growth extended so as not simply to involve the bladder wall and the pelvic bones, but it reached high into the abdomen above the umbilicus on the left side and there was another mass half the size of a man's fist bulged from beneath the liver. These masses were easily detectable and palpable after the bowels were emptied by a four-day fasting and enema regime. The posterior wall of the bladder was found on rectal examination to be one large nodular mass that bulged into the cavity of the bowel, nearly closing it. The circulation in the feet

was impeded by the pressure of the growth within the pelvis, so his feet were cold.

Treatment—Our glyoxylide was given February 16, 1931.

Results—Recovery progressed steadily until completed. He is now perfectly well over six years after treatment. Rectal examination reveals perfect normalcy. The bladder was opened about eight months after treatment was given because of calculi. The surgeon reported that the bladder was all healed, that no more cancer tissue was left, but that a more vascular area than the rest was present where the cancer had been. Seven months later the cystoscope was used and this area was seen to have the normal vascularity, and the bladder wall was found completely reconstructed. At this time the remaining calculi were removed. His health is normal.

CANCER OF THE VULVA

Mrs. K.—Age 44.

Heredity—Mother and two sisters died suddenly. Father died after three strokes.

Previous Illnesses—Pneumonia at 18 years of age and influenza in 1918.

Pre-growth Symptoms—Began to gain weight rapidly six years ago. A myxodematous condition gradually developed and she was put on thyroid substance, four grains a day. Peculiar spells of loss of control of the muscles, particularly of the arms and hands, gradually developed. Dizziness and susceptibility to pus infections and a general nervousness was present during the last six years.

In March, 1929, she noticed a mass in her right side

which definitely bulged and made it necessary for her to bend over when she walked. She was operated on and a small growth was removed from the labium, which was diagnosed microscopically to be a squamous cell carcinoma. The mass in the abdomen was not disturbed. Her health continued to fail. There was drainage with bad odor from the uterus. For the last few weeks she was sick in bed with pain in the right side.

Our examination made in April, 1931, revealed a large mass which involved the uterus and the surrounding structures, particularly on the right side. Rectal examination revealed that the mass bulged into the cavity of the bowel almost obstructing it. The tissue was characteristic of squamous cell carcinoma, such as it was found to be microscopically. She was rather weak and anæmic. Two cc. Ketene Solution was given and recovery was gradual, not being completed until May, 1933. The cancer growth had completely absorbed and the uterus was normal by March, 1932, but the thyroid function did not come to near normal until the spring of 1933. While under treatment, she was not given any thyroid extract and the thyroid gradually improved. There is a slight deficiency remaining which requires about a grain of thyroid extract a week to bring the thyroid action up to par. Of late the patient has found that this amount can be reduced, so we are expecting that in the course of a year or two the thyroid function will be perfectly restored to normal.

* * *

CANCER OF THYROID GLAND

Miss J. E.—Age 37.

Heredity—Negative to cancer.

Pre-growth Symptoms—For the last eight years suffered spells of aphonia for three-day periods twice a year. Throat troubled her for last three years.

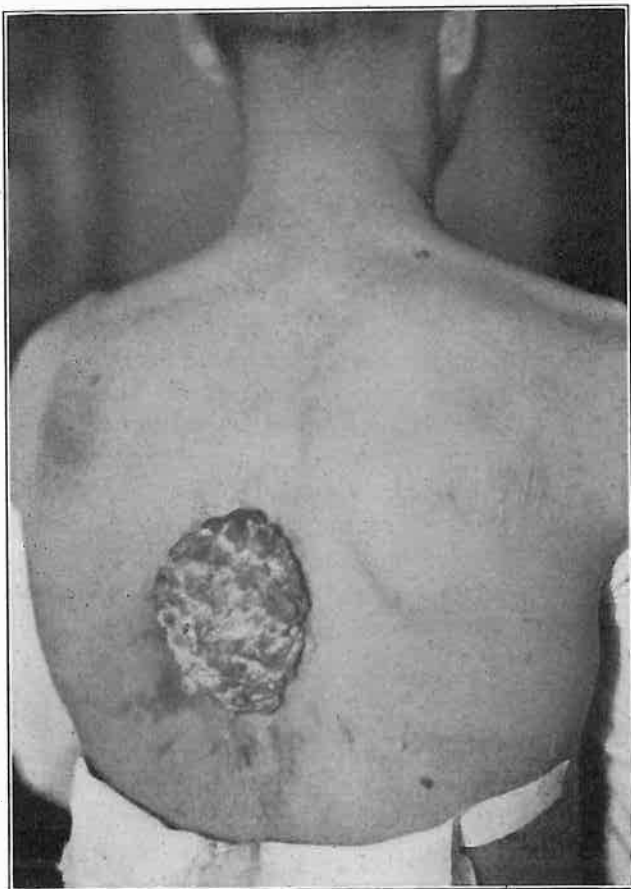
Present Illness—Started as enlargement of neck in the thyroid region in November, 1927. Biopsy was performed by Dr. M., December 2, 1927, which proved the malignancy of the lesion. There were no eye symptoms or tremor or any other indications of toxic goitre. The mass of cancer in the neck rapidly enlarged, pain became constant in the left knee, and a tenderness developed in the upper abdomen on the left side. Our examination revealed a typical cancer growth in the neck the size of half an apple. A mass about twice the size was found in the upper abdomen and above this mass the left rectus muscle was in a state of constant spasm. Tumefaction of the left knee produced definite bone irregularity. Thus the cancer tissue had reached the bone in the leg as well as glands in the abdomen where it was growing luxuriantly. The body weight was 169 pounds, showing a loss of only fifteen pounds.

Glyoxylide was given December 18, 1927, and recovery was rapidly completed, with complete absorption of all cancer tissue and restoration of normalcy in less than thirty-six weeks. Latest reports indicate that she is in perfect health.

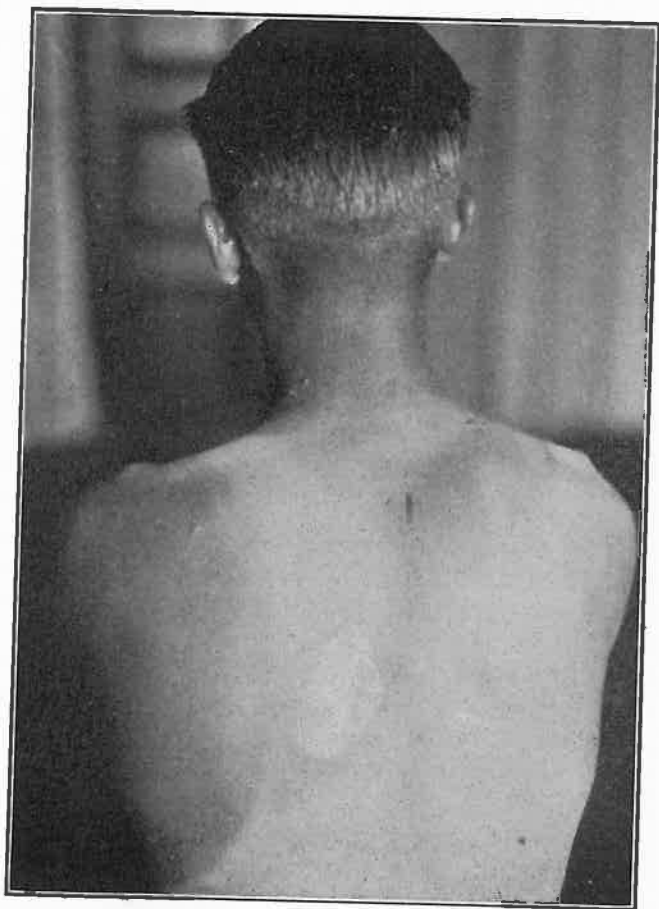
X-RAY CANCER

Dr. B.—Age 71. X-ray cancer developed between the first finger and thumb over an area the size of a

Inoperable well metastacized microscopically confirmed squamous cell carcinoma of the skin, refused operation at a reliable surgical clinic, made successfully operable by a dose of Glyoxylide.



Mr. L. after treatment when growth was undergoing digestion, just before removal. Note the areas of malignant pigmented infiltration which were not touched surgically. Also the two non-malignant pigmented moles on shoulder and right side.



Mr. L. after recovery, three months after treatment. Note the malignant pigmented infiltration disappeared, but the non-malignant moles still remaining though undergoing absorption and becoming smaller.

quarter following the use of X-rays for years in dental radiography. Radium and escharotics had been used unsuccessfully and at time of the Glyoxylide treatment it had been advancing steadily for some six months. Biopsy had confirmed the diagnosis, and amputation of part of the hand was being considered. However, one dose of glyoxylide under recommendation of Dr. D. was made on March 26, 1934. Recovery was steady and was completed in about eight months. There was also a great improvement in the general health. He remains well.

Dr. R.—Age 65. Had employed X-ray for a period of twenty years, following which, during the last five years X-ray cancer developed on the first and second fingers of the left hand; some malignant change showing on the thumb. The first finger was amputated after the pain had become so severe that it could not be stood and it proved to be X-ray cancer under the microscope. The second finger was under consideration for amputation too, because of the severity of the pain and the progress of the lesion when the Glyoxylide was tried in November, 1935. One dose proved sufficient and before a year passed recovery was completed with restoration of normal skin. The pain subsided rather rapidly. General health improved in many particulars also. He remains well.

CANCER OF BREAST

The following history is given in greater detail for those who care to study it.

Patient—*Mrs. C. N.*—Age 43. Housewife. History taken September, 1926, when Glyoxylide was administered.

Past History—Abscess of right breast following injury in childhood. Rheumatism at 13. Appendectomy in 1914. Gall bladder explored in 1920. Also tonsillectomy. Since 1920, enlargement of finger points, helped by colchicum.

Present Complaint—A hard mass above the nipple, egg size, first noticed in 1921, as a soft swelling which recently grew rapidly, large and hard causing retraction of the nipple. In January, 1925, right breast was radically removed with "axillary glands and pectoral muscle, carrying the dissection to the midline over the sternum upward to the clavicle and outward to the latissimus dorsi muscle, and downward including the upper part of the rectus fascia. The pectoralis major and minor were included. The microscopic examination made is reported thus: 1. Sections from tumor proper show larger and smaller gland alveoli lined with many rows of epithelium or entirely filled by epithelium. These cells are of moderate size and have relatively large deeply staining nucleus and many of them are undergoing mitosis. In addition to these large gland alveoli the fibrous atroma of the breast is infiltrated in all directions by compressed alveoli of the same type of cell. 2. Sections some distance from the tumor show hypertrophic gland alveoli and also large atypical alveoli like those seen in the tumor proper. 3. Other areas some distance from the tumor show no invasion, but alveoli containing large clear epithelial cells of the type designated "hyperplastic number 2" by McCarty. 4. Sections from nipple show no invasion. 5. Sections from axillary glands show large tumor alveoli in those from the midaxilla only. Diagnosis adenocarcinoma of breast." She left the hospital, February 12, 1925. The hospital reports their examination made, June 2,

1925 after a series of radiations from, February 9, 1925 to May 3, 1925, to show no evidence of recurrence. Likewise in July, 1925, no recurrence was noted. However, patient returned to the hospital in September with pains in the right subcostal region, nausea and vomiting. Examinations were reported also in November and December, 1925, and no recurrence mentioned except the possibility of liver involvement. In late 1926, the right arm began to swell, which her surgeons account for as due to lymphatic obstruction.

Examination—On applying to me in September, 1926, examination revealed a mass above the right clavicle a little larger than an English walnut. In the right axilla two tumors were found, one the size of a hickory nut and one the size of an almond kernel. The operation area showed some malignant induration as three small tumefactions in the line of suture. The liver was enlarged by three finger-widths below the right ribs as a definite hard mass attached to the liver. She was somewhat icteric in color. Very thin and toxic.

Treatment—One cc. of glyoxylide was given September 21, 1926. There was some definite reaction of grippiness, slight chills and fever several days later and during the third week. The metastasis absorbed completely before the end of the twelfth week. The large one above the clavicle disappearing first of all, namely, during the fourth week. In the meantime the gastric symptoms also cleared up and the liver involvement was no longer detectable after the sixth week. Her health improved steadily and her weight increased from about 87 to 103 pounds. Examination made in February, 1937, ten years after treatment shows no

involvement by cancer whatever and general good health.

Discussion—This case of very malignant cancer of the breast that recurred vigorously during the year following operation of the most radical sort, and deep X-ray therapy, made a prompt complete recovery on the Glyoxylide even though the recurrences were so widespread as to involve the liver as well as the glands and tissues of the operation area and above the clavicle.

MALIGNANT GLIOMA OF BRAIN

Mrs. T. R.—Age 35. Normal weight 209 pounds. Weight on admission about 70 pounds.

Diagnosis—By clinical history, X-ray and physical findings, malignant glioma of brain.

Family History—Negative to cancer.

Past History—She had a fever in Russia many years before, but was well otherwise until the present illness began in the summer of 1921.

Present Illness—The trouble started as headache, interference with vision and a gradual loss of the use of the right arm. In December, 1921, a piece of skull as big as the palm of a man's hands was removed from the right side. A diagnosis of glioma was made and two deep X-ray treatments were given. Her condition became progressively worse. A gradual swelling of the decompression area was observed. This increased until July, 1922, when we were called to see the patient. A hard mass as big as a grapefruit projected from the decompression area. The patient at this time was reduced greatly in body weight, paralyzed, blind and there was persistent projectile vomiting of the most severe type and massive liver metastases.

This was seven months after the X-ray treatments had been given.

Treatment—One cc. of Glyoxylide was given.

Results—Recovery was rapid. All traces of growths completely disappeared in five months, paralysis, vomiting and blindness disappeared and her weight was restored to 180 pounds. In another ten months her weight reached 220 pounds, where it stands today. She works hard every day. The bone removed from the skull has been completely reconstructed and there has been no return of the trouble. Seen last in July, 1936.

CANCER OF OESOPHAGUS AND CARDIA

Mrs. W.—Age 52.

Family History—Suggestive of malignancy.

Past Illnesses—Gastric ulcer for over twenty years with hemorrhages.

Present Illness—Started as rapidly increasing difficulty in swallowing and a bad gastric attack of vomiting and pains which did not cease day or night until laparotomy was done on November 7, 1936, after the pain had become especially severe. Laparotomy revealed a carcinoma occupying the whole lesser curvature of the stomach more than an inch in thickness; nodular, extending up through the diaphragm and reaching to the pylorus, and encircling the cardiac end where it caused constriction and obstruction. The width over the lesser curvature amounted to about five inches; length six inches. Radiographs previously and subsequently made showed two and one half inches of esophageal constriction and involvement. During the two weeks' attack she lost fifteen pounds, and some

ten pounds in the preceding few weeks because of difficulty in swallowing which reached the stage when even water would not pass. Her weight dropped to about ninety pounds by December 7.

Treatment of one dose of Glyoxylide given December 7, 1936 was followed by a few days of achiness and slight fever and chills. Thereafter, improvement was rapid with gain of weight and complete return to normal, functionally, radiographically, and by physical examination with gain of weight to 145 pounds. Splendid general health is fully restored.

LYMPHOSARCOMA

Mrs. A. C.—Age 40.

Family History—Mother died of cancer of the uterus at age of 62.

Past History—Appendectomy at 35. Had small lump back of neck size of pea from childhood.

Present Illness—Eight weeks ago lump began to increase to hickory nut size very rapidly and after five weeks had it removed surgically. Microscopic study revealed it to be "lymphoblastoma of lymphosarcoma type" as reported by pathologist of good standing. Rapid recurrence took place so that in three weeks the operated area became a tumefaction somewhat reddened and occupying the middle third of the Sterno-C-Mastoid muscle about an inch in diameter. Area below contained several masses the size of a pea and hard. There was rather rapidly developing toxicity and failure in general health. Loss of weight from 108 to 101 pounds in last few weeks.

Treatment—One dose of Glyoxylide was given on May 19, 1937 and recovery took place rapidly. In

Inoperable carcinoma of breast microscopically confirmed, and well metastacized, made successfully operable by several doses of Glyoxylyde.



Miss N. after growth started to become digested after the anti-toxin just before its removal.



Miss N. after complete recovery.

three weeks all tumors were completely absorbed and the weight gained to $102\frac{1}{2}$ pounds. Inspection, August 31, 1937, confirmed the recovery. Rapid recoveries take place in cases where the growth develops

rapidly and where the patient is not overwhelmed with the disease as this case illustrates.

CANCER OF UTERUS

It is easy to understand that a simple case of cancer, uncomplicated with serious deficiencies or injuries, may make a neat recovery and in the farthest advanced case where death is imminent and organic injury and vital deficiency have reached the limit, that recovery could hardly be expected. Still several such moribund cases have recovered for us on but one dose of the diketal that was given. An interesting case of this type that had been in final coma for twenty-four hours before she received the Glyoxylide and recovered, steadily and completely, is here sketched in the following history.

* * *

Mrs. M. P.—Age 47. Housewife.

Pre-growth Symptoms—Dizziness for twenty years. Double vision with overlapping of objects above each other apparently, from October, 1925 to July, 1927.

Past Illness—Cardiac lesion, mitral stenosis, for many years, with consequent cyanosis, dyspnea, etc.

Present Illness—Started as brownish discharge from uterus in fall of 1925. By June, 1926, tumefaction of lower abdomen, pain uterine bleeding and foul discharge. Examination by several surgeons and radiologists were made. Malignant infiltration found so widespread surgery was refused. Radium applied early in November, patient drove automobile then. Fourth radium treatment given on December 30, patient bedfast, had to be moved in ambulance. X-ray



BEFORE

Miss P. before treatment, showing metastases of recurrent cancer of breast over the clavicle, after surgical escarotics. There was also well developed metastasis in the axilla and infiltration of breast area.

then tried, declined in health even more rapidly; hemorrhages, pain and tumefaction increased. Examined at University of Michigan Hospital, diagnosis confirmed by biopsy, but refused treatment, sent home as hopeless. Two exhausting hemorrhages on May 29, 1927 completed her decline and by June 2, she was in coma.



AFTER

Miss P. after treatment with two injections of the "glyoxylide," showing disappearance of the recurrences. She has remained perfectly well with every trace of cancer abolished.

At this time the growth was enormous, filling vagina and compressing bowel, causing abdominal bulging.

Treatment—One dose of the glyoxylide was given June 2, 1927 while patient was in coma.

Results—Within a few days there was substantial improvement. Before the twelfth week she could work a bit in the garden. Within six months all cancer

tissue was absorbed. The diplopia disappeared soon after the Glyoxylide was given. She is perfectly normal now; no cancer; health perfect; except for the cardiac lesion. Weight normal.

CANCER OF UTERUS

Mrs. Mc. A.—Age 43. Housewife. History taken July 29, 1929.

Diagnosis—Made by clinical history, physical findings, exploratory laparotomy and microscopic findings.

Family History—Father's sister died of cancer.

Past Illnesses—She was rather healthy all her life except that since the influenza epidemic in 1918, when she had an attack, she was subject to stomach trouble. Pain in abdomen and right shoulder came in attacks that caused vomiting. Several doctors diagnosed gall bladder trouble and gall stones, but the X-ray did not reveal any stones. Nevertheless the attacks of pain were exactly like gall stone attacks, so she was placed in a hospital July 15, 1929, and an exploratory operation was made by Dr. T. He found a state of generalized cancer throughout the abdomen. The stomach, bowels and uterus were all involved. He removed a specimen for microscopic test which confirmed the diagnosis of cancer. Because of the hopelessness of the condition, he closed the abdomen and sent the patient to us for treatment.

Physical Examination—At the time of our first examination on July 29, 1929, the patient was in a state bordering on shock. On careful examination the great extensiveness of the malignant masses could be determined. Besides a large three-fist-sized bulging mass about the uterus, there were other smaller masses



Mrs. J. before treatment, note abdomen bulging in places from the growths within.



Mrs. J., abdomen returned to normal.

involving stomach and liver. Her heart was very weak and there was some cyanosis and dyspnoea.

Treatment—The Glyoxylide was administered on July 29, 1929.

Results—Recovery was slow at first. During the period between the sixth and ninth weeks there was constant vomiting and the already emaciated patient lost considerably more weight. In fact, several times we lost hope that she could recover. At the end of the ninth week she probably weighed about 75 pounds. After the ninth week reaction of chilliness and slight fever, she became able to retain food and soon started

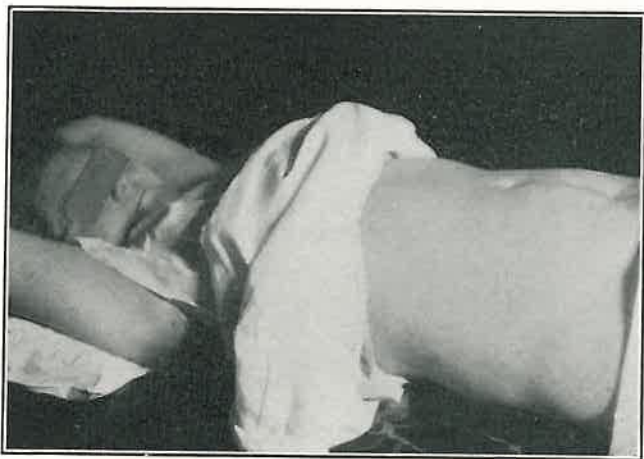


Mrs. McA.—Showing bulging cancer mass in abdomen before treatment. Diagnosed by exploration and biopsy far advanced cancer widespread throughout abdomen.



Mrs. McA. taken within six months showing complete recovery.

to gain at an appreciable rate, two and a half pounds a day for a while, then about five pounds a week and finally about two pounds a week until she about doubled her weight. After she reached 140 pounds, the increase was slow up to 180 pounds and thereafter still slower up to 200 pounds. All of the masses had absorbed by the time the weight increase was noted. She is entirely well. No trace of cancer can be found on most careful examination. She now weighs 220 pounds, more than six years after treatment, and is in perfect health.



Mrs. McA. taken in 1933 showing improved nutrition and complete recovery. She remains well still seven years after treatment.

CANCER OF RECTUM AND LIVER

Mrs. M. G.—Age 67. Housewife. History taken June 5, 1933.

Diagnosis—By history, physical examination, by exploratory laparotomy and biopsy, cancer of rectum.

Family History—Sister died of stroke at age 79. Mother died at 87. Father died at 77.

Previous Illnesses—Rheumatism of knees and ankles for the last four or five years. Thirty years ago had 18 pound fibroid tumor removed with the uterus. Good health since until two years ago when obstipation asserted itself and she concluded that she had a growth in the bowel. Examination by a good surgeon found a growth in the sigmoid in December, 1932. Obstruction became complete by April 27, 1933, when a "window" colostomy was performed, and a biopsy was made

that demonstrated that carcinoma of high grade malignancy was present. The patient so informed me but a search of the hospital records by the surgeon showed the biopsy report missing. A prognosis was made at the time of about a month to live.

Physical Examination—Examination June 5, 1933, revealed an enormous mass occupying and completely filling the lower bowel, palpable through the abdominal wall to be the size of a large cantaloupe. The liver was enlarged by a fist-sized mass, hard and lumpy, and bulging. Fortunately the colostomy was a lateral opening without severing the bowel. The patient was extremely cachectic and weak. Acopious drainage of foul bloody fluid and regular vomiting of food and decayed material was noted. The pain was very distressing.

Treatment—One cc. Glyoxylide solution was given on June 7, 1933.

Results—A reaction took place in three days, with some achiness. Thereafter there was improvement in her general health and less toxicity. The vomiting stopped. Soon she was relishing food and the pain left. By the end of three months some feces were passed per rectum, and in a year the colostomy healed spontaneously and all movements were discharged per rectum. She came to something approaching normalcy. Yet there was always some growth remaining and some discharge from the bowel. On July 30, 1934, a dose of Glyoxylide was given and thereafter a strong reaction took place, on the fourth day; and during the ninth and twelfth weeks, fever, achiness, pains in the abdomen and diarrhoea for a whole week. True recovery followed quite rapidly and she is in perfect health now, strong, free from cancer symptoms, and

without any growth traceable in bowel or liver. Her bowels move normally.

CANCER OF STOMACH COMPLETELY BLOCKING
CARDIA AND PYLORIS

Mr. B.—Age 46. History taken April 6, 1924.

Pre-growth Symptoms—Gastric ulcer for last ten years.

Present Illness—Started in 1921 with constant pain in epigastrium, radiating into dorsal vertebrae, vomiting of fresh and old blood, loss of weight from 220 to 120 pounds during 1922 and 1923, and suffered increasing pain on attempts to swallow, food returned quickly with blood. During last six months practically no food retained. Diagnosis made at several hospital clinics. Radiographs recorded complete involvement from cardia to pylorus. Confirmed by laparotomy March 12, 1924. Prognosis about one month. Thereafter became worse rapidly. On examination April 6, 1924, I found the belly scaphoid except for a large bulging mass filling the upper half and several smaller masses in lower half. Metastasis above the clavicle on left side, walnut size. No food could be retained, frequent vomiting of putrid bloody debris, extremely weak, suffered severely and was practically moribund.

One cc. glycolaldehyde solution was given subcutaneously. Recovery was steady, and within a year he was back to work and has been well ever since, except for an inguinal hernia sustained by heavy lifting. He gained to 200 pounds, works hard. Examinations reveal absolutely no pathology. Radiographs normal.

AUTOPSIED CASES

Several patients with extensive adequately diagnosed cancer within the abdomen were treated in the past and made full recoveries, but died from other causes than cancer. Autopsies were made to establish the cause of death and to investigate the possibility of recurrence of malignancy. They are briefly reported here.

CANCER OF UTERUS INVOLVING WHOLE ABDOMEN

Mrs. E. F.—Age 38.

Diagnosis—By clinical history and exploratory operation July, 1919.

Family History—Negative to cancer.

Past History—Well all her life until present trouble.

Pre-growth Symptoms—Dizziness and a sensation of falling long distances on closing the eyes, for a period of nine years before the growth could be felt in the lower abdomen by the patient. These attacks let up about six months before she noticed the growth.

Present Illness—Started with nausea, vomiting and pains in the back and lower abdomen, and attacks of pain that doubled her up. From July, 1918, to June, 1919, loss of weight from 172 pounds to 97 pounds took place and the growth in the abdomen enlarged until the patient noticed the umbilicus to be displaced to the right and become fixed. At the same time, the abdomen became large and hard and a change to a yellow cachexia took place. Several physicians made a diagnosis in June, 1919. Exploratory operation was

performed to settle the diagnosis and with the following report: "Found trouble to be cancer of the uterus, and in such shape that an attempt to remove it would undoubtedly prove fatal; consequently there was nothing to do but close the wound and keep the patient as comfortable as possible. Prognosis: six months."

At this time the body weight had dropped to 97 pounds. Patient kept failing rapidly, vomiting became continuous; pain constant, she became bedfast and several hemorrhages from the stomach took place. Patient was brought to Detroit November 17, 1919. At this time her weight was about eighty pounds; her legs were drawn up by the pain so that attempting to walk was made very difficult.

Physical Examination—Examination revealed a mass that involved all of the organs of the lower abdomen and pelvis and had also spread to the liver and stomach, causing frequent vomiting of blood.

Treatment—One cc. of solution of natural glyoxy-lide from heart muscle was administered intramuscularly in November, 1919.

Results—Recovery and complete absorption of the growth was completed in about a year and the patient remained perfectly normal and in the best health she had ever experienced until the Spring of 1935 when she sustained a cerebral hemorrhage. There were severe body bruises suggesting an accident. Autopsy was performed by Dr. W. The abdomen was carefully searched and no trace of malignancy found. The uterus and adnexia were preserved. They are free from cancer. A few days later an autopsy was made by the county coroner and the cause of death established to be cerebral hemorrhage.

In this case recovery from cancer, which was far

advanced at the start, was complete and permanent for over fifteen years without recurrence.



Mr. S.—Recurrent melanotic sarcoma after radium and escharotic removal before glyoxylide treatment given October, 1927.

SARCOMA OF ABDOMEN

Mrs. J. W.—Age 43. Housewife.

Diagnosis—By clinical history, physical findings, exploratory laparotomy and confirmed by microscopic examination, small round cell sarcoma.

Pre-growth Symptoms—Dizziness, headaches, and transient blind spells for some five years, that let up just prior to 1920, when disturbances, referable to a mass the patient felt in the region just above the umbilicus, became troublesome.



Mr. S.—Showing recovery after glyoxylyde treatment.

Present Illness—In the Spring of 1932 her legs started to swell and severe attacks of pain, that doubled her up, came at intervals. These attacks finally became rather frequent and were diagnosed as attacks of intestinal obstruction. At this time she could feel the growth that distended her abdomen and was referred to the surgeon for operation.

An exploratory operation was performed on August 7, 1922. A specimen was removed for microscopic diagnosis and the wound closed without any attempt at

removing the growth, which was found to extend throughout the abdomen. The surgeon thought she might live ten days and she was taken home to die. Her strength rapidly failed and in ten days she could no longer raise her hands to feed herself. At this time we were called to see her.

Physical Examination—Examination showed a large mass distending the abdomen and extending from the ribs to deep in the pelvis. Its size was much larger than a man's head. Both legs were swollen enormously because of the tremendous pressure of the growth on the large vessels in the abdomen. The patient was in great pain and very weak, suffering the cramps that characterize intestinal obstruction. The family was advised that it was most likely too late to obtain any results from the treatment as the heart was failing, but they wished to make the effort.

Treatment—The glyoxylide solution was administered in August, 1922.

Results—Recovery was gradual. She was back to her household duties within five months. All traces of the mass had disappeared, the swelling of the legs and feet had long since left, and her natural vigor had returned. She was in perfect health until the winter of 1927, when she developed pneumonia which caused an adhesive pericarditis. Thereafter a labored heart action persisted until death occurred by cardiac failure on November 20, 1928. An autopsy by three physicians demonstrated that not a vestige of cancer could be found and that the abdominal organs had been completely healed and reconstructed. However, examination of the heart explained its abnormal behavior for the past ten months and proved heart failure to be the cause of death.



Mr. R. before treatment. Note the bulging of the cancer masses throughout the abdomen. (History not reported here.)



Mr. R. after recovery—abdomen completely normal all traces of cancer masses have been absorbed.



Mr. R.—Abdomen drawn in to show the freedom from cancer growths. Recovery complete.

CANCER OF TONGUE

Mr. G. A. L.—Age 55.

Family History—Father died of cancer of the stomach.

Past History—Good health all his life except pre-growth symptoms.

Pre-growth Symptoms—Dizziness on stooping, lying down or getting up, spells of blindness and tachycardia, spells of loss of muscle control. These symptoms were much better after the growth came.

Present Illness—In the summer of 1923, noticed a growth under the middle of the tongue. He went to the University of Michigan Hospital where Dr. C. removed a specimen for diagnosis. Laboratory report: "Squamous cell cancer." September 15, 1924, the growth and part of the tongue were removed surgically

and radium applied. The radium was applied at monthly intervals three more times. The second radium treatment was followed by a more rapid extension of the growth, which was increased with each subsequent radium exposure. Finally in March the cautery was used radically after the last radium application. In three weeks the disease spread with terrific speed, so as to involve the whole mouth, palate and cheeks. The lower jaw bone was exposed and largely necrotic. The base of the tongue was represented by a large cancer mass that occluded the pharynx, preventing any attempt at speech or swallowing. The sides and front of the neck and chin region were entirely infiltrated and swollen hard and blue. The patient was practically bedfast and emaciated and suffering severely. Hemorrhage was severe. First glyoxylide was given April 11, 1925, and the second May 12, 1925.

Results—In one week after the second treatment patient was able to take heavy liquid foods without aid and the extension of the disease over the cheeks had cleared up. Three weeks later patient was taking regular diet conveniently. Reconstruction of the jaw bone and tongue were satisfactory after one year. By September, 1925, cure was completed. Patient back to work at the automobile plant where he had been employed before his illness. Gain of nearly 55 pounds in weight.

In the summer of 1931 he fell while out walking, was taken to the hospital in an unconscious state and so remained for three weeks. The doctors could not satisfy themselves as to the diagnosis. He came out of the state of unconsciousness suddenly and soon was back to work, but shortly afterward another spell of the same kind proved fatal. Autopsy revealed that there

was no trace of cancer to be found anywhere in his system but that the brain cells showed a hydropic degeneration characteristic of radium injury. Thus though he was cured of cancer by the antitoxin, radium injury still progressed to fatality.

Recoveries demonstrated at autopsy as long as fifteen years after treatment certainly speaks for its permanency.

SURGERY AS ADJUNCT TO THE KETENONES

In the recovery from cancer under this type of treatment it may prove a convenience or a necessity to surgically remove the growth. Thus when the patient must work and odor is a disadvantage, or if a large badly infected mass of necrotic material would tax the body resistance too severely, surgical removal of the major accessible growth material after immunity is established may be done. Two photographs with brief statements as to history have been submitted to illustrate,—pages 130, 131, 138, 139.

There is always risk of irretrievably destroying recently induced immunity when anaesthetics must be used. Therefore, whenever possible, recovery should be attempted without taking that risk.

ALLERGIES OF THE CONTRACTILE MECHANISM

In both coronary occlusion and obliterative endarteritis besides the allergy to such toxins as that in tobacco which excite the angiospasm and the hypertrophic response in the cells of the intima, the pain of the vascular spasms and muscle spasms occurring with occlusion and circulatory failure are due to the presence of incompletely burned materials produced by muscle contraction in the absence of a supply of oxygen and glucose. In such areas the oxidation catalyst must also be exhausted, and a fresh supply behaves specifically in reducing the pain and correcting the pathology. The spasms and hyperplasia of the original allergic response are quickly corrected and sufficient circulation is soon restored to the part to burn up the pain producing products of muscle spasm through the catalysis of the glyoxylide. The toxic substances and their effects are thus removed and with reasonable time the whole pathology is corrected.

A few case histories illustrate.

CORONARY OCCLUSION (THROMBOSIS)

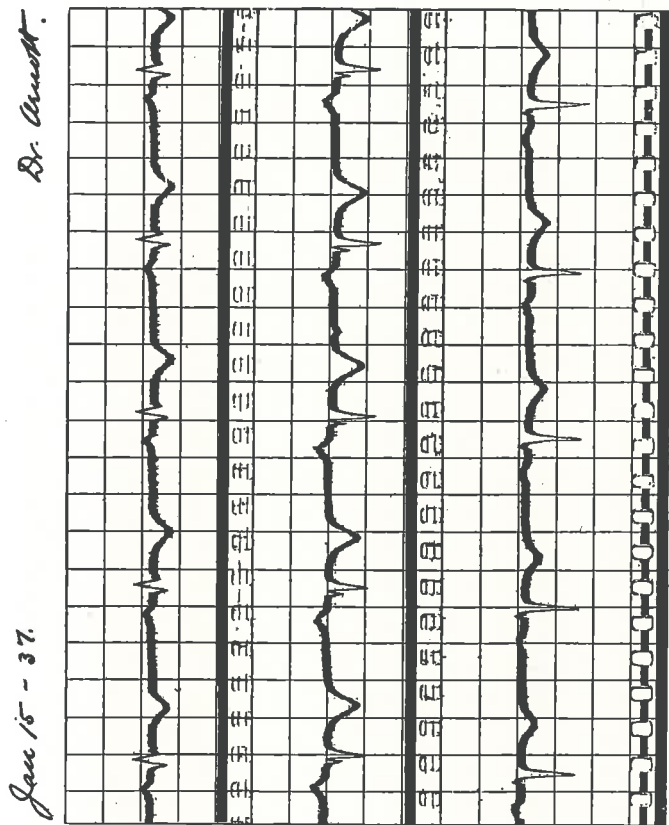
Dr. A.—Age 64. Brisk and active habits. First attack occurred while walking Dec. 2, 1936, and passed in a few minutes after resting. Dec. 4th an extremely severe attack of pain while resting. Repeated heavy doses of morphine, hyperdermically influenced the pain only when sufficient to stupify him profoundly. Dec. 8

Glyoxylide was given subcutaneously, followed by very considerable relief within an hour. Eighty-four hours later another dose of Glyoxylide was administered, after which the pain soon entirely disappeared, and at the time of writing, has not returned. A careful convalescence was observed, and he has been restored to good health, and able to live his ordinary life in comfort.

Five weeks later an electrocardiogram was taken which showed a grave condition due to coronary thrombosis though all pain had been relieved. Nine weeks later a second electrocardiogram showed a normal condition. He now is in good health, reasonably active, and free from any symptoms of his old trouble.

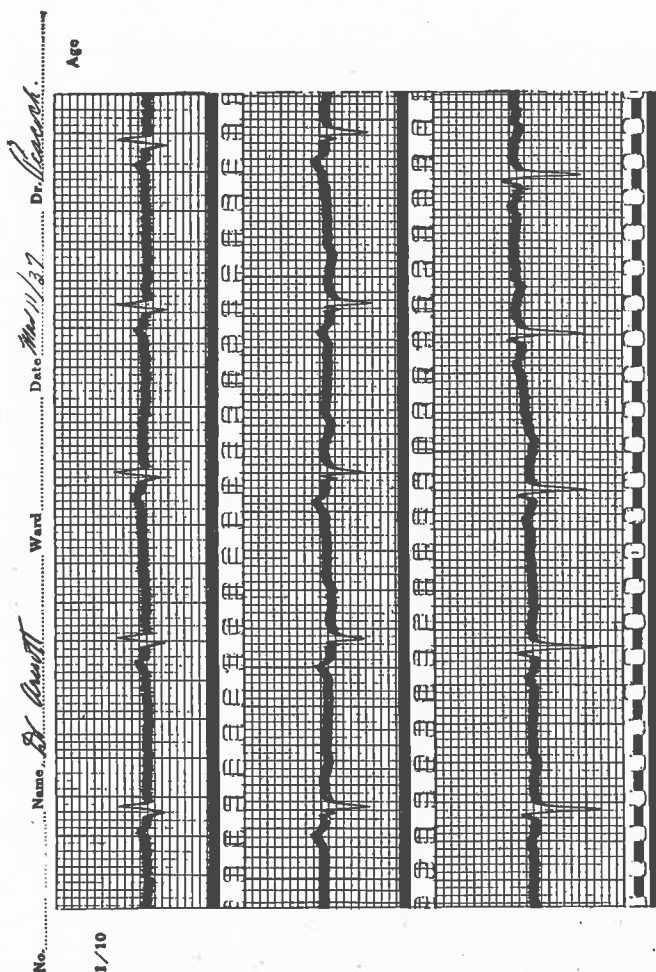
CORONARY THROMBOSIS

Dr. B.—Age 58 at time of treatment, January, 1926. In this case the coronary thrombosis was complicated by marked arterial and coronary sclerosis, as revealed by radiographs and electrocardiographs. Patient had been a busy country practitioner up to 1917 when angina pectoris pains compelled him to cut down on his work. They came on exertion and after eating. At the end of 1925/ pains were so commanding as to prevent any work and it was impossible to walk a hundred feet even very slowly without precipitating one or more attacks. In January, 1926, one dose of the diketal as prepared from fructose phosphoric acid, was given intramuscularly in the arm. Recovery was steady so that in three months he resumed his practice with comfort, and gradually came to normal which he still is.



No. 1. Electrocardiogram made five weeks after treatment when pain was entirely gone.
March 11, 1937.

Dr. A.



No. 2. Electrocardiogram taken eight weeks after No. 1 when recovery was established.

Mrs. H.—Age 74. In February, 1936, had marked symptoms of angina pectoris. Careful dieting and quiet habits were observed with considerable relief but was obliged to be in bed most of the time for several weeks during the summer of 1937.

December 6, 1937,—a sudden seizure with very severe pain in the chest revealed a condition of coronary thrombosis, and rest in bed did not relieve the pain, which at times was agonizing. The Koch Glyoxylide was administered December 11. On December 12 the patient reported very marked relief and in three days no more pain bothered her while resting except slightly after her meals. This soon disappeared also, and in a fortnight she was able to go to the bathroom without causing any return of symptoms. At the end of six weeks she reported that for a fortnight she had not required any hot water bottle to her feet, night or day, though there was cold winter weather, and during the summer of 1937, while confined to bed, she had been obliged to have hot water bottles to her feet constantly night and day.

She is able to move about the house quietly, symptom free, and in a general way feeling better than for two years previously.

Mrs. B.—Age 51. Failing health prompted a rest away from home for three months but no benefit was received. On her return severe repeated colds, painful joints in her hands, shoulders and knees obliged her to remain in bed for three weeks. Bronchitis with profuse expectoration, sometimes blood-stained with marked dullness in the upper left chest suggested the presence of lung cancer since no TB germs were found in the sputum.

X-ray of the chest revealed a dilated heart and

aorta, and no growth or TB lesions, so a diagnosis of "An arterio-sclerosis affair" was the report of the x-ray reading.

Koch Glyoxylide injected November 11, 1937, gave such help in six days that 90% of the symptoms had disappeared. She now is about freely with no signs of bronchitis since three weeks after receiving the Koch treatment.

One could not fail to notice that her habitually blue tinged lips had become normal in color in a few days and continued in satisfactory condition.

ADVANCED ARTERIAL SCLEROSIS

Mr. P.—Age 93.

Quite well most of his life, was a painter by trade. High blood pressure and attendant usual symptoms increasing in degrees for years. Quite feeble for last two years. In the fall and winter of 1932 several "strokes" and a complete spastic paralysis took place making him perfectly helpless and stupid; an extreme case of senile paresis. This state remained until April, 1933 when a dose of Ketenes was given. At this time the arteries were tortuous, nodular, and hard generally. Improvement was evident in a month, and in seven months his mentality had returned to normal. He was also able to walk about and dress himself. In a year he could do some work about the house. In the meantime the blood vessels became smooth and elastic, the tissues lost their cyanosis and the elasticity of the skin and tissues also returned. He remained well and active for three years that I knew of.

Two things are to be noted, first that the cause of the pain is removed by removing the pathogenic toxin

through the restored oxidation mechanism. This is promptly accomplished. Secondly, the pain is not the result of the arterial sclerosis, which is consequent to the causative factor like the pain. Since the sclerosis is a stubborn structural change it takes a longer time to be removed and corrected. Both the pain and the sclerosis are removed by the same mechanism that restores the normal function for the dilated heart return to good tone again, though not as quickly as the pain goes. In other chronic toxic states like tuberculosis with dilated heart a good tone is restored more rapidly than lung is restored or the body becomes completely free from germs. We may say then that the pain causing factor is the toxic factor that causes the myocardial weakness and lowers the resistance to infection, and causes the sclerosis.

It is found that acetyl choline produced at parasympathetic nerve endings during their function, prevents the accumulation of fat in the liver on heavy fat and cholestrol feeding, when injected into the body in such minute dosage as one to ten million. One is inclined to look upon an exhaustion of its function by fatigue and failure in its production as a cause of cholesterol deposition and of the changes that regularly follow in the degeneration of the vessel wall; whereas an over-production with consequent vessel spasm and impoverished circulation in the wall accounts for coronary spasm and the changes that are consequent. Since the excess acetyl choline is normally burned and destroyed by a normal mechanism, in the presence of good oxidation catalysis, no harm can come, but where this is lacking coronary spasm follows. The key to recovery here is the restoration of normal oxidation catalysis, which burns up the acetyl

choline not used. But the action is deeper here as it also is in the other conditions where actual degenerative changes are going on in the vessel wall, for the toxin causative to the crippling of the oxidation mechanism and the ability to produce acetyl choline is also burned up, and the pathogenesis of both states is nipped at its source.

ANGIONEUROTIC OEDEMA

Mr. J. H.—Age 23. Angioneurotic oedema of lungs, larynx, whole face, and even the cornea. Stridulous breathing. Dyspnoea came on suddenly after quick change in temperature from hot to cold. Vision obscured so that automobile head lights looked like pin points. Tremendous swelling and apparently complete obstruction to breathing. Condition seemed almost fatal for a half-hour before glyoxylide was given intramuscularly. In less than two minutes relief was perhaps 80 per cent. Recovery complete within one hour.

OBLITERATIVE ENDARTERITIS

Mr. K.—Age 50. Treated July, 1928. Obliterative endarteritis, both legs and feet to the knees. Much pain, bedfast. Amputation at knees requested by surgeon. Blood sugar 380. One dose glyoxylide followed in three months by much improvement and in six months by complete recovery. Blood sugar 80. No return of trouble. Patient died recently after a fall. Autopsy was not permitted.

LUETIC DERMOGRAPHIA

Mrs. F.—Age 37. Syphilis since 1922. Tertiary stage. Skin and mouth lesions. Angioneurotic oedema and dermatographia outstanding symptoms. Resistant to usual antiluetic treatment. Blood Wassermanns repeatedly positive and not influenced by forced antiluetic treatment. Large welts developed at easy pressure or slightest rubbing. Marked welts on stroking skin. One dose potassium glyoxylide solution given, November, 1935. Recovery complete in six months. Three Kahn tests taken at three-month intervals were negative each time. Patient enjoys the very best health. No lesions or skin pathology. Very slight hives sometimes.

ASTHMA AND HAY FEVER

Mrs. R.—Age 45. Multiple sensitivity. Grandfather had asthma badly. Severe cystitis nearly continuously for twenty-five years. Resisted all treatments given. Hay fever, asthma, severe sinusitis, generalized, pigmented, itching hives constantly. Skin tests showed hypersensitivity to over one hundred different substances. Fifty of which were immediately and extremely toxic, dermatographia. No help from various treatments. One dose of glyoxylide was given in May, 1934. Recovery complete in all respects within six months.

ALLERGY OF THE SECRETORY MECHANISMS

The above described case of asthma and hay fever demonstrates that where the allergy was of long duration, personally and hereditarily, recovery may require a long time too. A case of hay fever of short time duration illustrates how rapidly a case of allergy of the secretory mechanism can recover.

Mr. L. K.—Age 48. Regular autumn hay fever for last ten years. Had to go North for relief. Suffered quite badly. After suffering for two weeks in Fall of 1934, one cc. of glyoxylide solution was injected at four in the afternoon and the next morning he awakened without distress and remained free from all allergic symptoms to date.

Mr. J. L.—Age 50. Father had asthma. Patient had asthma for ten years, in which time he could not draw a full breath. Much secretion and spasms. Constant dyspnoea, especially on exertion. Could walk stairs with difficulty only. One cc. malonide solution given September 8, 1936, was followed by total freedom from symptoms in about three weeks. Has gained thirty pounds in weight since and is perfectly normal. Climbs hills without discomfort.

Mr. A. L.—Age 23. Hay fever and asthma several years with increasing severity so that he had to leave the environment during the pollen season. One cc. of glyoxylide given in July, 1935, before attack came conferred immunity so that a month later he worked in the field thrashing right in the blower dust

without the slightest indication of an attack. He has remained well ever since in spite of exposure.

Correction of allergy of a ductless gland is well illustrated in the following case.

Mrs. W.—Age 58. Several years of nervousness. Tendency to perspire easily. The gradual development of extreme exophthalmus, tremor, dyspnoea, and bronzing of the skin. There was vomiting with loss of weight from 150 to 108 pounds in one year. Examination revealed also an oedema of feet and legs and the presence of a hard fixed mass bulging from and filling the epigastrium. One dose of glyoxylide was given, September 28, 1929. Recovery was complete in about sixty weeks. She remains in perfect health to date. Normal in weight and all respects.

We have here a recovery from advanced Cancer of the stomach with mediastinal secondaries and severe thyroid and adrenal disease. The daughter of this woman, who was thirty years younger, developed a brain tumor after severe head injury. Almost constant convulsions characterized her case at the time she received a dose of glyoxylide—also in 1929. Recovery was completed within two years and is permanent. Their homes are in the goitre belt of Ohio, yet normal thyroid function returned under the same conditions where its pathology developed.

ALLERGY OF CENTRAL NERVOUS SYSTEM

DEMENTIA PRAECOX

Mrs. D.—Age 50. Treated January, 1923. Dementia præcox with delusions of persecution lasting some six years following six years of anxiety neurosis, ten years of gastric ulcer, symptoms followed in the last two years by steady development of a massive carcinoma of the stomach palpably about the size of a grapefruit at time of treatment. Delusions that "needles and pins were put in food and drink to kill her;" could see them. Feeding forced at times. Bed-fast. Recovery was complete in two years after two injections of glyoxylide solution. After recovery patient was asked about delusions, she stated, "She knew they were not true, but nevertheless could not help believing them, head was very woozy anyway." Therefore, in spite of her physiological judgment the delusion held sway allergically, dominating the mind. She remains well in all respects. Abdomen normal.

DEMENTIA PRAECOX

Miss W.—Age 44. Colitis for twenty years. During last twelve years dementia præcox and recently spells of pain in abdomen without palpable pathology, delusions, and compulsion neuroses. Prolonged periods of violent dementia. Ten doses of potassium glyoxylate and two doses of Glyoxylide in the course of the last three years established an apparent recovery.

ALLERGY OF THE SENSORY NERVOUS SYSTEM

My attempt to produce an allergy of the sensory nerve endings in 1914 with synthetic fluorescent substances yielded success with a substance closely allied in structure to adrenalin and to caffeic acid, a dihydroxy benzene compound with an unsaturated side chain as its bromine derivative. A dilute solution without showing any visible change, vasomotor or otherwise sets up a continuous burning sensation of several days duration that cannot be removed by washing. It never failed to produce this effect a short while after being applied to the skin. Its close similarity in structure to adrenalin is interesting.

The neuritides are frequent precancer symptoms. The greatest variety of such cases have recovered by use of the glyoxylide.

SHINGLES (*Infective Neuritis*)

Miss J. K.—Age 12. Showed lesions of Herpes Zoster which had been present three days. Pain had kept her awake for four nights. Treatment was given at noon July 23rd and was followed by relief. She slept well that night and the pain never returned. The red base upon which the blisters rested had given place to normal color when seen twenty hours after the treatment was administered. With the exception of two small superficial scabs and the loss of the sun-tan over the affected part, all physical signs had disappeared in another week.

ACUTE NEURITIS OF SHOULDER GIRDLE

Mrs. C. W..—Age 40. Pain in shoulder girdle very severe for two weeks, kept her awake most of each night and she suffered severely during the day as well. Twelve hours after one dose of glyoxylide, pain was permanently gone, recovery complete.

EPILEPSY

In spite of the multiplicity of factors making up the diabetes an epilepsy complexes, the essential allergic nature resident in certain nerve centers seems well supported by the facts so far assembled. A case of diabetes was already reported; a recovery from epilepsy will serve to illustrate.

Miss B..—Age 17. School girl. Epileptic fits for over three years, occurring at night after retiring. Most often when observed, Aura centered about stomach. Not more than three fits a day, sometimes but once a week. On dose of glyoxylide solution given August 12, 1929 was followed by a gradual recession of the disease, so that by the twelfth week only a few petit mal were observed and thereafter recovery became complete, with no more fits.

One institution for defective children recently treated a series of epileptics, and found that about 50% of the cases, treated with one dose appeared to recover in about six months, while the response in the others was not so definite.

PSORIASIS

Miss N.—Age 32. Brother has psoriasis. Patient had tonsillitis one and one-half years ago. Tachycardia on changing posture soon followed and one month later psoriasis started on thigh and spread rapidly in spite of expert concentrated attention. At the time of glyoxylide injection body was generally covered, hair and nails affected. Ears almost separated from scalp. Recovery completed and heart action returned to normal fourteen weeks after one injection of glyoxylide given, April 2, 1926. Recovery is permanent to date.

The photographs of two other Psoriasis patients are presented here also. In each the disease was general, affecting the skin, scalp and nails. They responded rapidly to treatment and after about one year of apparent recovery, relapsed to nearly the original state. Another treatment again secured recovery, which so far as I know, remains permanent. It seems that psoriasis is typically slower to recover than cancer. This is exemplified in the case of a far advanced case of cancer of the stomach, with a large bulging mass that caused frequent severe hemorrhages. There were several metastases to other parts of the body, and an earlier long standing psoriasis. Recovery from the malignancy was prompt to a dose given in May, 1924, but the psoriasis took about two years to completely disappear. He is in perfect health to-day.



Plate No. 5.—Showing psoriasis lesions in Miss N. before treatment.



Plate No. 6.—Showing recovery from psoriasis after the glyoxylide treatment.

THE INFECTIONS

The following common serious infections have been quickly overcome in animals and in men by restoring vigorous oxidation through the catalytic activity of Glyoxylide: distemper, pneumonia, severe *Staphylococcus pyogenes aureus* meningitis, acne, common colds, arthritis, sinusitis, Vincent's infection, acute anterior poliomyelitis. Depending upon the chronicity, syphilis, leprosy, and tuberculosis have recovered rapidly or slowly.

The virus infections uniformly respond quickest so that in measles, with 105 degrees fever, with severe eye and ear symptoms the temperature may moderate in one hour, and be normal next day and the patient feel very well in two days.

In severe shingles, relief from the pain and inflammation may only take hours, and the blisters and ulcers soon show healing. In malaria, with regularly recurring attacks, one dose may stop further attacks permanently. A post-operative *staphylococcus meningitis*, that was apparently terminal showed improvement in a few hours but took several weeks to recover, and an acute Neisserian infection in a woman with most virulent cervical smears, was germ free two days after treatment. Rapid recovery depends upon high toxicity and the predominance of polymorphonuclears. The lymphocytic stage demands more time and the macrophagic stage still more time.



Case No. 61.—Mr. E. front view before treatment, showing extensiveness of the lesions—even the palms of the hands, and the nails were affected.



Case No. 61.—Showing front view after treatment.



Mr. C. before treatment.



Mr. C. after treatment.

ACUTE ANTERIOR POLIOMYELITIS

Only two cases will be reported here, one a child of two years, presenting characteristic symptoms prodromally and paralysis of both legs, feet, and thighs for forty-eight hours before treatment of one dose of glyoxylide. Recovery was complete with normal return of muscle control within twenty-four hours. No atrophy followed. The other case was a boy of seventeen. All muscles of torso, legs, thighs, arms, neck, the internal rectus of right eye, the swallowing muscles, the diaphragm, intestines, and urinary bladder were paralyzed. When treated with glyoxylide paralysis of whole right leg was already established for four days, and paralysis of the other muscle groups took place within that time, until respiratory paralysis was just about complete, and cyanosis deep, patient unconscious. Recovery started to show within ten minutes after the first injection, noticed in the straightening of the right eye, slightly better breathing and diminution of the bloated abdomen, and the return of swallowing within a day. He required catheterization for four weeks. Satisfactory restoration of muscle development and control required about two years with reconstruction of right rectus abdominalis muscle and right femoris still going on.

TUBERCULOSIS

Miss A.—Age 16. Advanced tuberculosis of both lungs. Spontaneous pneumothorax, left chest. Heart shifted to the right side. Massive tuberculosis left kidney. Evident tubercular meningitis. Projectile vomiting every few minutes for three weeks, cyanotic.

Fever 105. Pulse very weak and rapid. Bedfast. Treated one dose of Ketenones, July, 1922. Recovery took two years. Whole left lung regenerated. No more pathology traceable. Heart restored to left side. Married has healthy twins who are very resistant to colds. Health is still perfect.

Mr. K. L.—Age 27 years. Single. No family history of tuberculosis.

Always well until in the summer of 1932 when he contracted pleurisy after sitting on cold cement block while perspiring. Recovered and felt well until in May, 1935, when he developed a pleurisy pain in the right side which lasted for several weeks. After an x-ray examination of the chest at that time he was admitted to the Herman Keifer Hospital for tuberculosis. In July, 1936, he was given a crush of the right phrenic nerve at that hospital.

He presented himself here for treatment September 4, 1936. There were no active symptoms except that he had failed to gain in weight. His normal weight was 153 pounds and since his illness began it had remained at 143 pounds. Physical examination of the chest showed adventitious breath sounds in right upper thorax and in the right axilla. There was no change in rhythm and there was no indication of cavity formation.

He received a treatment of Koch's Ketenones on September 9, 1936. September 25 he weighed 149 pounds and there was some improvement in the breath sounds on the right side. November 27 he weighed 151 pounds. His pulse was 88. February 15, 1937 his weight had increased to 156 pounds and it remained the same until he went to work in April.



Mrs. R. (Miss A.) and twins born after her recovery. These children inherit immunity demonstrated in total freedom from colds.

The breath sounds were normal and have remained such. July 19, 1937, after doing manual labor for four months, he weighed 161½ pounds and had no symptoms of tuberculosis.

Mr. J. O.—Age 36 years. Mexican laborer.

Coughed all winter but felt better in summer; had night sweats sometimes but did not feel feverish. No history of hemoptysis. Has been losing weight for several weeks and feels so weak he cannot work.

Physical examination—Kyphotic spine, pallid complexion, deep supraclavicular fossae, slight decrease in resonance in upper left thorax and left apex, no rales heard, no change in rhythm of breath sounds anywhere but appear greatly diminished in volume over entire chest, pulse 86. Normal weight 150 pounds—present weight 130 pounds. (See x-rays.)

Diagnosis—Advanced chronic pulmonary tuberculosis fibrotic type involving both lungs. Contraction of upper left lobe and numerous cavities. Scattered areas of infiltration in both lungs.

Progress—Patient received intramuscular injection of Ketenones January 25, 1937 and was put to bed. Cough rapidly disappeared, appetite improved, and by March 11 he had gained 16½ pounds in weight. Examination on this date showed improved aeration of right lung, no rales, but diminished resonance and breath sounds over upper left lobe. Pulse 86. Patient anxious to go to work.

On April 5 he weighed 152 pounds and was free from symptoms. Pulse 76.

An x-ray taken on this date showed a decided decrease in the areas of density.

April 12 he weighed 155 pounds. Pulse 72.

April 19 completed 12th week from date of treatment. Weight remains 155 pounds.

He is out of bed, able to take long walks without fatigue, and is free from symptoms. Advised to go to work.

May 15, weight 154 pounds. Has been doing light manual labor for nearly a month with no loss of weight and no return of symptoms.

Mr. R. O.—Age 25 years. Occupation: Job-setter. Oct. 1, 1937, reported well and working.

Awakened at 3 a. m. July 24, 1936 with a coughing spell and raised about two ounces of blood. Had a medical examination and was told the x-ray showed tuberculosis of the lungs. He had a moderate rise of temperature in the evening for three days.

Examination of the chest on July 31, showed no change in resonance. There was an increased expiratory sound in the upper right thorax and some subcrepitant rales. (See x-rays.) There was no afternoon fever on this day. His weight on that date was $137\frac{1}{2}$ pounds—normal weight 140 pounds.

At a prior examination made at the Herman Kiefer Hospital he was given a diagnosis of active pulmonary tuberculosis.

Progress—He received treatment on July 31, 1936. August 13 he had gained three pounds in weight and had no afternoon fever during past week. He still had a slight productive cough. Auscultation of chest was negative.

August 20—Cough gone. Walks a mile every day but takes rest hours. Weight 140 pounds.

September 17—Weight 142 pounds. Pulse 70. No rales in chest with expiratory cough.

September 28—Weight $142\frac{1}{2}$. Pulse 94.

October 8—Weight $143\frac{1}{2}$ pounds. Pulse 86.
Walks two miles every day.

December 3—Weight 144 pounds. Pulse 99.

December 22—Weight $144\frac{1}{2}$ pounds. Pulse 60.

January 21—Weight 147 pounds. Pulse 100. Ordered to bed for three weeks.

February 18—Pulse 86.

March 18—Weight 152 pounds. Pulse 78. Walks several miles every day.

April 15—Weight 152 pounds. Pulse 88.

May 20—Weight 152 pounds. Pulse 64.

June 1—Weight $149\frac{3}{4}$ pounds (summer clothing). Pulse 88.

July 1—Weight $153\frac{1}{2}$ pounds. Pulse 72. Playing tennis and golf for past month. Goes to dances. X-ray shows marked improvement. Advised to go to work.

October 1, 1937—Weight 161 pounds. Free from symptoms.

Mr. C. M.—Age 20 years. Single. First symptoms observed were those attributed to bronchitis, coughing and raising in early part of 1934. Had been told repeatedly that his tonsils were diseased and August, 1934 the tonsils were taken out. Soon after this operation he began having night sweats, raised blood in sputum, had dizzy spells and occasionally mild headaches. There was a rapid loss of weight at that time and he went from 127 pounds down to 118 pounds. Later with rest in bed his weight went up again to 150 pounds.

Physical examination of chest showed a slightly decreased resonance in an area two inches in diameter in the second and third left interspaces at the mid-clavicular line and in the left paravertebral space

just above the angle of the scapula. There was no change in breath sounds except slightly diminished in this area with faint sibilant rales heard occasionally in this region. His weight was 141 pounds; normal weight before illness was 127 pounds. An x-ray of chest showed an increased density in the right apex, an area of calcification and consolidation in the left hilus region corresponding to upper part of lower lobe.

Treatment with Koch Glyoxylide was given on January 12, 1937 and he was restricted to moderate activity with rest hours.

February 1—Weight 142 pounds. Pulse was 76. No symptoms.

February 8—Weight was 145 pounds. Streaks a little in morning. Can take long walks without fatigue.

April 19—Weight was 154 pounds. Raised sputum streaked with blood during twelfth week. Walks five miles daily without fatigue.

April 26—No cough and sleeps well. Weight was 154 pounds.

September 4—Reports he has been working for past three months without symptoms.

Mr. T. D.—Age 49 years. Married. Patient stated he experienced severe headaches twice a week for many years and had "sinus trouble" since 1918.

Two months ago he began coughing and after an x-ray examination he was told that there was a lot of old scar tissue. His cough persisted and on January 2, 1935, he had a severe hemorrhage. His doctor advised him to have his lung collapsed and to go away for a year.

His present weight (January 31, 1935) was 130 pounds. Normal weight was 135 pounds.

On physical examination of the chest there was an

area of decreased resonance in the upper left thorax and apex. The expiratory breath sound was heard loudly in this area and there were loud rales present. These signs of a large cavity in the upper left lung were confirmed by x-ray.

Treatment was given January 31, 1935.

On February 13, 1935 he complained of chills and fever and a productive cough.

March 6, he reported he had had chills and fever for two days in the previous week. Weight had increased to 139 pounds, four pounds more than at any previous time in his life.

May 11, weight 144 pounds. Had moderate fever in ninth and twelfth weeks since treatment. States he has not had a headache since treatment.

October 23, weight 151 pounds. Had a hemorrhage in last week of July. In the 33rd weeks of his treatment he had a fever of 102 degrees for two days and lost five pounds. Has been doing manual labor for past four months.

June 30—Weight 156 pounds. He has been working steady although he had a sharp fever reaction in the 48th and 60th weeks. Physical examination shows little change from original condition.

On March 25, 1937, although his general condition continued to improve and his weight had increased, while working, to 162 pounds, he was given another treatment because the x-ray showed the cavity to be still persistent. At the present time, September 15, 1937, he is working and has no symptoms of any tubercular activity, nearly three years since his first treatment.

The above cases typify the rapid uninterrupted recovery that follows the administration of Koch's Ket-

enones where there has been no previous sanatorium treatment and ill-advised collapse therapy. In Case No. 5 the recovery was somewhat more prolonged although steadily progressive for two reasons: First, the disease had been of much longer duration and more fibrotic changes had taken place in the diseased lung. Secondly, the environmental conditions were more adverse because of the fact that the patient felt compelled to earn a livelihood for his family.

SYPHILIS

Mr. K.—Age 32. Treated, November, 1923. Syphilis of throat. Resistant to vigorous usual anti-luetic treatment. Throat badly swollen and ulcerated. Voice lost. Skin lesions generalized. Blood Wassermann persistently positive. Condition growing worse over a year. One dose glyoxylide was followed by complete recovery in three months. Blood Wassermann negative thereafter. Remains well.



Gumma of skull B. W. 4 plus, confirmed by biopsy. Appearance before the treatment was instituted. (Courtesy of Prof. Maisin.)



Six months after first of three injections. Complete recovery. B. W. negative negative. (Courtesy of Prof. Maisin.)

ARTHRITIS

Resembling the allergic lesions of lues, tuberculosis, leprosy and malignancy, in both rheumatoid arthritis, and in osteoarthritis advancing hyperplasia followed by necrosis is the rule. The picture is that of an unsuccessful response to infection. The restoration of a vigorous oxidation catalysis even in advanced stages with extensive ankylosis and much pain and necrosis has brought about a recovery to about ninety per cent of normal. The following cases illustrate.

Mrs. T.—Age 74. Rheumatoid arthritis for nearly thirty years, progressive until all joints including the jaw articulations had become firmly ankylosed, and terrifically painful on touch or tension. Most joints were distorted, fusiform in shape, enclosing hypertrophic inflammatory deposits and covered with shiny skin. One dose of glyoxylide was given in December,

1927, pain was soon better and in three months she was able to walk a few steps. In one year recovery had become about ninety per cent of normal and has so remained.

Mr. A.—Age 60. Poker spine with rheumatoid arthritis. Painful hypertrophic and atrophic ankylosis of practically all joints including jaw articulations progressing for the last two years with occasional exacerbations. Tonsils had been badly infected for a long time; pyorrhea, sinusitis, and myocarditis present. Treatment of one dose of glyoxylide given in January, 1937; started a rapid subsidence of pain, with absorption of hypertrophic deposits and restoration of ability to walk and open mouth. During the twelfth and fifteenth week reactions, exquisite tenderness accompanied a healing restoration of joint tissues after which perhaps a ninety per cent return to normal was established with improvement still going on.

TUBERCULAR ARTHRITIS AND OSTEOMYELITIS

Miss S.—Age 20. Tuberculosis of left knee joint for fourteen years. Three operations between ages of six and twelve to relieve acute flare-up of osteomyelitis in lower half of femur shaft. Distortion of bone progressive with increasing ankylosis and deformity. Motion angle ten degrees. The fourth flare-up took place in July, 1934, with swelling and intense pain of the knee joint. Rapidly progressive. Could not walk. Radiographic study revealed 'irregular structure and contour of lower third of shaft of femur' with defective calcification and bone absorption, clouding of articular surfaces narrowing of joint space, extensive proliferation around periosteal border. One dose of

glyoxylide given July 23, 1934 was followed by rapid decrease in the pain and a steady restoration of joint and bone to normal, functionally and structurally, with perfect use of leg and full motion within nine months. General health has become excellent.

ARRESTED DEVELOPMENT

An interesting case of arrested development is that of a boy 14 years of age, Mr. S. He was a characteristic picture of infantilism with the feminine form of small shoulders, large hips, delicate skin and hair and female voice. Neither testicle had descended to the scrotum and he was rather fat for his height of 5 ft. 2 in., weighing 150 pounds. Treatment was given and in two years he grew to 6 ft. $\frac{1}{2}$ in. in stature, broad shoulders, small hips, very muscular with a boy's voice and male hair distribution. The testicles had both entered the scrotum and had developed to normal dimensions. Thus full development of the sex glands was restored through the re-establishment of the normal oxidation catalysis and a normal development and physiology were accomplished.

Mr. D. H.—Age 9. History taken December 30, 1929. Past illnesses measles, whooping cough, chicken pox, and enlarged tonsils that were removed in 1935. Cataracts of both eyes since the age of six. Present illness, vision practically nil after four o'clock in the afternoon, could not see windows. Restless writhing motions. Contraction of left arm. Both eyes completely cataractous. Right eye turned downward. Hemolytic color. These conditions showed no change since six years of age. One dose of glyoxylide was given December 30th, and apparently complete recov-

ery followed. Febrile reaction within three weeks and eyes were completely normal by March 20, 1930. Vision apparently completely restored. Mentally normal also. Arm normal. Writhing motions completely disappeared. He became a normal child, quite intelligent. Subsequent reports indicate a complete recovery.

In this instance as in multiple sclerosis, there is definitely an allergic hyperactivity of some nerve centres expressed in the choreiform movements and hyperreflexia. These states may be interpreted, of course, as cerebellar activities escaping deficient cerebral control. But this interpretation has not been proven, and would require that a restoration of nerve tissue takes place in the recoveries we have observed. It is easier to think of a toxic hyperactivity of the neurones involved, rather than a choking off of control impulses by scar tissue, or a failure of development of cerebral tissue, since in both cases the recovery response is too rapid for scar dissolution or new nerve development.

Functional abolition of eighty years standing, in nerve tissue, may also be corrected by the unsaturated ketones. The instance is a physician of eighty-three years of age when taking the treatment for senile epitheliomata of the face. He had been totally blind in the right eye since three years of age, and was becoming so blind in the left eye that he discontinued practice. He recovered. Nine weeks after the injection he reports that the eyes are both able to see a string at a distance of ten feet, each eye tested separately. The condition was diagnosed choroiditis by each of a large number of eminent ophthalmologists throughout the country, who stated the condition was beyond help.

RECOVERY PERCENTAGES

The percentage of recovery results, vary with attending factors. In advanced to far advanced tuberculosis, Dr. Gerrit Warnshuis reports in a series of eighty-five cases under continued observation, on an average, more than one year, there was a total mortality of fifteen which is less than twenty per cent, as compared to the usual sanatorium mortality of ninety per cent for cases of this type. These figures assume great significance, particularly since all fatalities were among cases so far advanced and rapidly progressive that no hope could be entertained for them to live more than from a week to a few months and the cases which responded favourably included many nearly as far advanced, and progressing toward fatality also.

In leprosy, treated in the Belgian Congo under Professor Maisin's direction, as high as seventy per cent of mild cases are either healed or germ free within three months. In cancer some physicians are pleased with a recovery percentage of twenty to thirty per cent in advanced cases involving the vital organs, and some report as high as eighty per cent of recoveries where the series includes selected cases of early and moderately advanced stages of the disease. In my own experience I have seen comparatively simple cases at times not recover while utterly hopeless far advanced cases that could not turn in bed because of weakness have made rapid and permanent recoveries, following but one dose of glyoxylide (35). Evidently influences not easily defined in terms of involvement or exhaus-

tion have a definite bearing on the recovery process and hence statistical analyses must be exhaustively complete and complex to convey an accurate estimate.

Like recovery percentages, the speed of recovery depends upon various factors. Thus an otherwise totally resistant angina may clear up slowly after one dose, and a regularly recurring malaria attack may never return after but one dose, while a chronic malaria ranking with syphilis in its ravages may require months and repeated dosage for recovery.

The more primitive the structure and function affected, the more specific must the pathogenic agent and the more active the curative agent be to produce their effects. Thus while I find that the cyclic dihydroxy unsaturated caffeic acid inhibits oxidations mildly in a general way, very specific types of unsaturated quinone structures are required for carcinogenesis. Their toxic effects upon the oxidations supporting the reticulo-endothelial system are reflected in the loss of proper crenating ability of the red blood cells, or rather in the failure of the spleno-lymph system to remove abnormal cells. Where this power is low one can hardly expect proper destruction of cancer cells or germs either. Indicative also are the blood ph and oxidation-reduction potentials. I find the latter to estimate around 4 mvs. for so-called normal people, and about 5 mvs. in some cancer and chronic luetic patients. With recovery it may drop temporarily to as low as 3.3 mvs. Improvements in such features may facilitate early predictions, but the fundamental complexities involved require recovery percentages to be estimated late after treatment.

CONCLUDING STATEMENT

No simple statement can be comprehensive enough to cover the chemistry of immunity, but a few matters set forth here should be recalled. Chief among them is the importance of the carbonyl group to the oxidation process, be it for function or the burning of poisons. In the amino acids the carbonyl group is quite inert since it is flanked by an amino group. In this way the protein structure is protected, but when a toxic state is brought about through bacterial or some other action, immunity does not emerge until a sufficient degree of protein lysis and desamidation takes place to liberate a quantity of carbon chains possessing carbonyl groups. The efficiency of the carbonyl yield thus accomplished will depend upon the molecules that carry this group. When carbonyl is flanked by hydroxyl, by another carbonyl, or by an ethylene or acetylene group, I have found its catalytic powers to be greatest, and that is why we have proposed glyoxylide as the most efficient immunity body possible. Malonide is definitely effective against malignancy and the most severe infections, and propargylic aldehyde, containing both a carbonyl and an acetylene group has proven curative in very severe infection. Hydroxyl or another carbonyl (dihydroxyl) in close relation, are also accelerators of carbonyl activity. Thus in cancer we have found glycolaldehyde and glyoxal able to restore a sufficiently vigorous oxidation mechanism to produce true recovery; and any agent that can correct the deficiency in cancer can do so too in all the other allergies and infections. Thus immunity depends upon simple bodies containing carbonyl groups that are properly associated with hydroxyl, carbonyl, or unsaturated carbon unions. No single structure carrying carbonyl is curative in every case. In the instances described below two simple structures proved very effective, but they failed in other instances. The whole group previously outlined are required to cover the usual run of cases of all diseases. Disease producing bodies when derived from the amino acids must lose their carbonyl groups as in histidine, or in methyl guanidine, derived

from creatine. The negative catalytic effects of bacterial toxins have occasion to arise here and in the further unsaturated imino groups. To demonstrate the lasting restoration of immunity secured by carbonyl groups alone or with hydroxyl where the patient was in the most extreme state of depletion, two case histories are offered solely for emphasis. Highly diluted formaldehyde solutions have yielded definite benefits in true malignancy also.

Mr. H.—Age 51, April 25, 1925 when examined and treated. Past history of gastric ulcer with severe hemorrhages for fifteen years and recently a severe myocarditis. Present illness started in 1924 as vomiting, pain in stomach area and rapid loss of weight. In last four months lost from 178 to 155 pounds. My examination revealed a bulging mass occupying the epigastrium and extending 2 inches below umbilicus, metastasis to left supraclavicular space. One also in anterior shelf of sigmoid, mediastinal dullness increased. Radiographs demonstrated lesion extending from prepyloris to cardia and cap absent. This was constant in all films. Patient was cachectic, cyanotic and dyspneic; much hemolysis. One dose of glycolaldehyde solution highly diluted was given intravenously. Recovery was steady. All pathology cleared up within a year. He works hard and remains well.

Mrs. E. R.—Age 57 at time of treatment, November 6, 1923. She had an advanced inoperable cancer of the uterus and was refused surgery at the Mayo Clinic in June, 1923, and sent back home as incurable in November, 1923. My examination made November 6, 1923, revealed a mass of cancer that bulged like a six-month pregnancy, extending to one and one-half inches above the umbilicus. The mass expanded the vaginal vault and obliterated the cervix, was nodular, hemorrhagic and draining. It extended throughout the adnexia and involved the bladder wall, causing much compression. It had grown rapidly since June. General marked arterio-sclerosis, and some skin pigmentation disturbance. One dose of glyoxal solution was given; improvement started on the fourth day and she steadily gained $\frac{3}{4}$ -pound per week from 115 to 168. In six months the whole cancer mass had completely absorbed. She remains well to date.

SUMMARY

On the basis of deficient oxidation catalysis, therefore, a broad field of pathological expression exists, which may affect each and every cell structure and function.

The allergenic and physiological import of free valency in regard to peroxidation, polymerization, and ketogenesis in normal and toxic substances depends upon molecular structure and oxygen status.

The pathogenic feature thus resides in the specific photochemic behavior of atomic free valency where it exists in appropriately constructed molecules. Aside from theoretical and experimental data, this is demonstrated clinically by the restoration of normal structure, function, and immunity through a vigorous oxidation catalysis. The measures employed are the intermediaries of the two types of aerobic glycolysis I have proposed here to be the carriers of the oxidation chains. They are prepared synthetically and injected intramuscularly where convenient. They change the toxic type of structure to that which they possess while they are active. They restore the coagulation phase (Tissue Thrombin¹²) of digestion of abnormal blood and tissue cells, and activate the various oxidation enzymes, the hormones, and vitamins. Restored vigorous oxidation eliminates both primary and secondary disease causes and permits normal tissue reconstruction and function.

The recovery process is rhythmic and self-perpetuating. That it can often be established in advanced stages of serious disease, functional, structural, and infectious, is here exemplified with clinical reports.

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