


Nutrition and Glands in Relation to Cancer

By

F. E. CHIDESTER, A.M., Ph.D.

Nutrition
and
Glands
in
Relation
to
Cancer

—
CHIDESTER



This Book Tells You

Why fear of cancer is being reduced

The truth about hereditary cancer

How one may overcome a tendency to cancer

Why delayed examinations and treatment are
fatal

How we are now reducing the mortality in
cancer

What promising research brings most hope in
cancer treatment

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Nutrition and Glands in Relation to Cancer

By

F. E. CHIDESTER, A.M., PH.D.

*Consultant in
Nutrition & Endocrinology*

For many years, all over the world, men and women of courage, with great hearts and high hopes, have labored and died in their efforts to bring about better knowledge of the prevention, treatment and causes of cancer. All their efforts were made available to this writer. His work has been made more effective by the great opportunities always offered to the people of the Americas, North and South. Descended from maritime ancestors with sturdy bodies, and traditions of agricultural and professional pursuits, we fight for the right.

Evidence is presented which will help the physicians in their treatment of cases; will evaluate and clarify research for the investigators; and will bring hope for prevention and guidance for living to the general public. We have merely assembled the "Acres of Diamonds" including our own.

Each person has a right to full credit for his part in the experimental work and the enormous job of correlation. We acknowledge with happiness that our own studies have been necessary.

Lee Foundation for Nutritional
Research

Milwaukee, Wisconsin

Announces

**Nutrition and Glands
in
Relation to Cancer**

By

F. E. CHIDESTER, A.M., Ph.D., F.A.A.S.

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and Surgery, Newark, N. J.

Sometime Fellow, Clark University, University of Chicago, Major-Sn-Res., U. S. A., Member, Order Military Surgeons, U. S. A., Organizer of Curricula in Public Health, in 2 State Universities, Consultant to Clinicians, drug and food firms, and in Cancer Research, University of Michigan. Author of "ZOOLOGY"—D. Van Nostrand Co., 1932, and many journal articles. An explanation of the role of minerals, vitamins and glands in the origin, prevention, and supportive treatment of cancer.

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NUTRITION AND GLANDS IN RELATION TO CANCER

By

F. E. CHIDESTER, A.M., Ph.D.

*"They must upward still and onward
Who would keep abreast of truth."*

JAMES RUSSELL LOWELL

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DEDICATION

*Dedicated to that most valuable, least recognized
and poorest paid group,
the general practitioners of medicine*

"But nothing is more estimable than a physician, who, having studied nature from his youth, knows the properties of the human body, the diseases which assail it, the remedies which will benefit it, exercises his art with caution, and pays equal attention to the rich and the poor.

Voltaire—"A Philosophical Dictionary"

Preface

This book began about fifty years ago, when, as a small boy, I helped mother hunt up references to the most recent literature in journals and annuals for my father who was, I now learn, a rather remarkable physician.

The great driving force in all the enormous work of correlation has been the desire to do good in the world, and, despite a lack of the medical degree, to carry the torch that was laid down by my father, a pupil of Nicholas Senn. He was a truly great physician, whose remarkable cures were not appreciated by me until my own experiments led me back to his application of the fundamental principles of the chemistry of medicine. Some of these principles have been obscured by fads, or obfuscated by ads.

Father cured pernicious anemia, leukemia, pneumonia, and many skin diseases, he was an expert on prenatal care and pediatrics, and he was a pioneer in the use of diphtheria antitoxin in his county. (In upstate New York, always give the "caounty.") But his skill extended to wonderful surgery of tumors, and the treatment of certain ulcers with cancer signs by ferrous iodide internally and acetic acid externally. Iodo-acetic acid slows down tumors.

I have set forth in my paper, "A Doctor's Son Looks at Mental Healing," published under the name Wadsworth Stephenson, certain facts regarding the old time doctor who knew medicine, and from whom emanated conscious power, because he *did* know. "The Doctor had come."

Without many years of experimentation in the fields of embryology, mineral balance, endocrinology and pharmacology, this writer could not have made his correlations. Teaching postgraduates, public health students, and premedicals for more than 20 years paved the way for work with clinicians, and for actual cancer experiments.

A policy of unselfish devotion to a great cause has not brought this writer any notable grants, nor has it insured large returns in

payment from drug and foods firms for his summaries. But it has enabled clinical men to save lives, and the correct evaluation of research and clinical findings in published papers has brought letters of appreciation for belated recognition of remarkably valuable studies by others. In some instances, mine was the only crediting publication, and therefore was emphasized in their minds more than ordinarily. Everyone needs encouragement, at times.

Even the most distinguished surgeons, radiologists and cancer research men have such keen consciousness of the antagonism and jealousy which their finest efforts provoke that they are pathetically grateful for honest recognition by others in published articles. This antagonism is a real one which goes along with the strife for priority and improved opportunities for work, in many active fields. Among many of the members of various organizations such as the Pathologists, Surgeons, Radiologists, bitter arguments have arisen, and cancer work has been poorly served by their unwillingness to get together. For there is a common ground, and only preoccupation with the details in each field has prevented its discovery. Individual effort is necessary, but the correlation of discoveries is eventually the key to truth.

“Employ your time improving yourself by other men’s documents. So shall you come easily by what others have labored hard for.”

—SOCRATES

THE WAY OF THE CORRELATOR IS NOT EASY

A year ago, an old friend said to me, “You are not the only one with these ideas about cancer, are you?” The reply was, “No, thank God, and every one of the living men with similar ideas has been an active correspondent, and whenever possible has looked over the sections of this book on which he is an authority.”

Doctor W. Mitchell Stevens, of Cardiff, Wales and I click all the time and his ideas are backed by thirty-five years of clinical experience. A while ago I could not stand it any longer without making some more mouse tests and tried to get a project going under the

aegis of the dairy people on iodizing the mice that belonged to cancer strains so as to inactivate the cancer that their nurslings develop. My letter to the dairy people was mailed at almost the same day that Dr. Stevens sent me one from Britain, urging the same program. I got his letter two months later. Thought transference? Maybe, but "chance favors the prepared mind."

Others will determine the extent to which the writer's own experimental work, correlations, and discussions with clinicians have aided in the fight against cancer and allied diseases of metabolism.

It is the aim of the author to present facts regarding the inter-relationship of body-chemistry to the conditions which permit cancers to develop, and to show the importance of proper medication and diet as adjuncts to surgery and radiations.

We have tried to bring such accurate knowledge before the public and the physicians that there will be "HOPE WITHOUT SELF-DECEPTION," which is the slogan for the recent book, "The Robe," by Lloyd Douglas.

It is well nigh impossible to prevent frantic patients and their even more disturbed relatives from trying any remedy that they hear will benefit cancer.

As Dad wrote his son Dave, also a physician, in the *Medical World*, November, 1935, "If you were told tomorrow by the most eminent physician you know that you were an incurable case, and that you would live but a few months, the chances are that, in spite of your medical training, you would do just what these ignorant people are doing, seek some irregular practitioner who promised something. You would not sit with folded hands."

The same journal editorialized on cancer, "We can imagine no greater contribution to terrified humanity, as well as to the patient sufferers from this dread disease, than the thought that something tangible and understandable is being done to banish this cloud from the bright skies of health and happiness."

While cancer has had the reputation of being an "old-age disease," *Radiology* (1943) reports that in Massachusetts, in 1939, the death rate from cancer in children was higher than for pulmonary tuber-

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culosis, measles, diabetes, scarlet fever or typhoid. Of the 150,000 persons who died of cancer in the United States in 1939, approximately 1,100 were less than 15 years of age.

We believe that proper nutritional and glandular balance in the prenatal period, as well as in early childhood, will prevent cancer in children.

WHY CANCEROUS PATIENTS DO NOT CONSULT PHYSICIANS

Just before World War II the *Swiss Medical Weekly* asked 93 cancer patients why they had delayed seeking medical attention.

- 26 cases developed so rapidly that it was too late to save the patients by the time the disease was discovered.
- 18 patients had believed their ailment was harmless because they had no pain.
- 14 kept at work, fearing inability to take long leave for convalescence.
- 13 were suffering at the same time from a relatively harmless disease, and attributed their symptoms to the other disease.

- 7 patients feared an operation and postponed seeking medical attention.
- 7 women had false modesty about diseases of the reproductive system.
- 2 had consulted physicians previously when nothing was the matter with them, and feared that they might be classed as hypochondriacs.
- 3 were lazy and indifferent.
- 3 were addicted to faith healers.

On this basis, we have no record of the cases where speedy death after treatment for cancer has frightened friends of some patient, also in need of operation.

Nor have we the explanation that many women *expect* to suffer from some female disorder, and hence do not realize that they may be actually developing a malignant growth, when in pain.

The author had been engaged in teaching and experimentation in the fields of Biology and Public Health for 25 years before he began gathering evidence about cancer. Having established the fact that iodine is the key to the action of the glands of internal secretion, he was impressed by the remarkable studies of Gen. Sir Robert McCarrison, on the fat-thyroid-iodine balance, and was able to show how vitamins, glands and minerals are inter-related.

In 1933, when actively engaged in furnishing material to a national group of clinical-correspondence clubs with 50 branches in 30 states, he decided to undertake experimental and clinical studies on cancer, and other sterol-induced diseases. An opportunity was given to work in this field at the University of Michigan, where every facility and encouragement that one could ask was granted. In 1934, a committee from the medical and scientific faculties, and the Director of a great Michigan Foundation sponsored his application for an annual appropriation of \$50,000. But the five medical projects were all refused. Christian Science won. Yet this writer believes in mental healing *with* medication and food.

Since governmental funds for cancer are in general allocated only in very small amounts to persons *outside* the regular staff, a well sponsored application for \$75,000 for a three years' clinical and experimental study of endocrines and cancer was refused by the U. S. Public Health Service.

The correlations presented have been a labor of love, for it seemed that relatively few persons had the background of experimental work and knowledge of the literature to undertake it. But the heart warming responses from clinical men, who have written for information, and who have been good enough to acknowledge aid in their work through reprints on loan by the American Medical Association Loan Library, have in themselves been encouraging.

In the meantime, as a consultant on vitamin-mineral-gland relations, drug firm and foods company affiliations have enabled the writer to present his views unaltered, in widely distributed articles.

It is most gratifying to record the fact that those who have in their practice developed similar views have through mention in the writer's articles been given an opportunity to extend their usefulness in publications and in addresses to scientific and medical societies throughout this country.

The public would be amazed and indignant if the facts were fully set forth regarding the noble men who have until recently endured ostracism, and braved attempts to have them disbarred from practice of medicine, because they dared to suggest any measures in cancer other than the orthodox surgery and radiant energy treatments. But

now the scale is turned, and we find research on the rôle of the vitamins in cancer to the fore. Moreover, since others with the writer have directed attention to the significance of glandular therapy, and the dangers of *synthetic* hormones, some of the foremost investigators in the field of endocrinology have cautioned the medical profession about using the very preparations that they developed.

The attitude of the majority of drug firms on the *vitamins* is well expressed in one advertisement by a U. S. firm. We omit the name of the drug firm. "The present spectacle of vitamin advertising running riot in newspapers and magazines, and via radio, emphasizes the importance of the physician as a controlling agent in the use of vitamin products. We feel that vitamin therapy, like infant feeding, should be in the hands of the medical profession, and consequently refrain from exploiting vitamins to the public."

Some of the best known cancer authorities are still unwilling to consider any relationship between dietary or vitamin deficiency and the incidence of cancer. One of these men (a self-publicized director) actually used with some success the lead-iodide treatment of Bell, without registering the fact that the iodine played any part. His mind was closed!

I am greatly indebted to radiologists, surgeons, and endocrinologists who have read those sections which lie within their fields. There are now a number of clinicians who have applied in their practice the dietary and mineral supplements which we have indicated as valuable in cancer or precancerous conditions. These cancer workers are mentioned in the text.

If those men who have adopted as their own the suggestions made by me since 1933 regarding supportive treatment, and those others who have been so good about criticizing and correcting sections of this book and the various journal articles which preceded it, wish to make public their approval, that will be fine. But I shall not give their names as unwilling sponsors.

Our own preliminary unpublished tests with mice were too few and thus have been of no statistical value, although in all probability as important and complete as some of the "tests" made by critics who "failed to confirm" the laboriously prepared experiments of some who

were to be summarily "disposed of" in reviews. We have merely tried to help physicians in human cases where *supportive treatment* after operation or radiation was indicated.

Now we shall see what the dog-in-the-manger fringe of authorities have to say. They not only can see no hope but apparently have such thick skulls that no new idea can possibly penetrate. They call this conservatism. I refer to those stupid ones who would demolish the results of years of work with the senile but cryptic comment "rot," or who have written scathing and utterly unfair reviews of strategic papers, trying to "convey a libel in a frown, and wink a reputation down." Swift said that, but these men are not swift. "Au contraire" they have been barnacles too long, while people died in agony, and others not favored by their influence stagnated, became frustrated, and gave up.

"To pray together, in whatever tongue or ritual, is the most tender brotherhood of hope and sympathy that one can contract in this life."

—MADAME DE STAEL, "CORINNE"

I feel that the prayers of my father and mother, and a number of priests and Protestant ministers, together with their parishoners, have enabled me to do three men's work for a great many years. I have credited many people, but my own fundamental research is basic to all of my conclusions. And, I announce with much humility that I believe that God has guided me in all of my good deeds, while the Devil, with my personal aid, has been responsible for my pure cussedness.

Since I was told in 1934 (just after the Rackham Foundation plan to let me use the income from one million dollars fell through) that I had done the greatest job of correlating in the past 100 years of medicine, I have been working and also praying that "they" would see. Now, I have set forth the facts so clearly, and so many times in so many ways that they *will* see. If a man is willing to give all that he knows to the world free, they'll take it, use it, and then give him no credit. Such matters have been common in my experience for some time.

I prefer to have the reputation which has caused two distinguished friends to scold me, and to arrange it so that in my talks, the basic discoveries made by my fiercely loyal students and myself were given decent mention.

Now, I launch this book, in which I have set forth honestly and fairly, and with as much clarity as I can, those facts which will, I pray, be helpful to doctors and research men, and will bring Hope to the frightened public.

Shortly after this book is published there will be once more (for I have issued papers on cancer) a flood of letters from all over the world, demanding that I help the writers or their relatives. I shall not attend to any such letters. I am a hard working individual who *cannot* practice medicine.

There are undoubtedly a few medical men who have followed closely the series of papers on vitamin-mineral-gland balance, and on cancer, that this writer has published. Some of these men will ask for help, even from a Ph.D. of the teaching group. If it is possible to assist in *hospitals*, with the warm sympathy, keen interest and understanding of my former students and research aides, many of whom are in the armed forces, that will be done.

Since my body is aged prematurely by unrecognized hard work, I shall conserve my brain power, and regulate my work, sleep, play and food without interruption.

In the United States of America, we should follow Richard C. Cabot's thesis, "What Men Live By" and WORK, LOVE, WORSHIP, PLAY, with the happiness that goes with right-living.

If pressed by the public, or annoyed by reporters, I shall immediately go on the air to the people and demand peace in order that I may rest and do my stuff. For my correlations on diabetes, polio, and insanity have already been applied, and I don't know the end. Perhaps it will be like the earnest visitor to the art museum, who mistaking his labels, and seeing a gigantic Scot of more than mature years in one picture, and an old hound in another, read "There's life in the Old Dog yet."

Earlier workers with the extracts from glands of internal secretion did not realize the importance of the *iodine* in such glands. Even

today, we find an alarming tendency to ignore the fact that the synthetic *sex hormones* may cause cancer, unless they are accompanied by thyroid extract or iodine. *The American Medical Association Journal* has warned repeatedly about such powerful drugs.

In any program of supportive treatment for cancer, it is most important that we view with interest new medicaments, which may be successful with animals, but hazardous in human cases.

"If a man will begin with certainties, he will end with doubts; but if he will be content to begin with doubts, he shall end in certainties."

—BACON

You remember the little boy who, when asked what good deed he had done, said, "Why, I saw a man standing on the bank of a river and smiled at him." That man did not commit suicide, it was learned later, just because the boy had smiled. We don't want people to kill themselves because of the unnecessary agony from futile radiations or from fear of preventable diseases.

I had crushing grief over the deaths of a few dear friends in West Virginia from glandular trouble and then inquired into matters a bit more thoroughly. Yet, before I went there in 1919, I had received a substantial offer as Research Director in endocrinology. Teaching is better if you get family histories and can help. Besides there are all those fine medic's, scientists and ag's who appreciate one's help and interest. One of these men, after driving 80 miles to hear me talk to a clinical club in Toledo, said in the presence of two of my medical sponsors, "If you'll only get me just enough to eat, I'll go anywhere in the world to help you put these ideas over." There are probably 500 medical and scientific graduates with that same spirit, upon whom I might be able to call. Hospitals need ideas, and men with ideals, and *they have them*—make no mistake about that.

One of the young college girls whom we all admired and who died from preventable gland trouble, was of that not too numerous type of real lady, who, as I told my students, "met you in the morning, smiled at you and you were happy all day." Let's keep our children from evil, train them in right and healthful living, and to go the right way. Then let's follow the same way ourselves once in a while!

Juvenile delinquents have delinquent parents. Syphilis, alcoholism and low moral tone pave the way for disease, and disease means death.

If this book does its duty, lives will be saved. My own poor life is in it. God Bless You!

LIFE IS A MISSION. EVERY OTHER DEFINITION
OF LIFE IS FALSE, AND LEADS ALL WHO ACCEPT
IT ASTRAY—EVERY EXISTENCE IS AN AIM.

—MAZZINI—LIFE AND WRITINGS

F. E. CHIDESTER,
*sometime Major-SN-RES., U.S.A., an
Member, Order of Military Surgeon,
U. S. Army; fellow, Clark University
and University of Chicago.*

Woods Hole, Massachusetts,
September 25, 1944.

Acknowledgments

Many persons, consciously or unconsciously, have helped in the preparation of this book. The writer is especially indebted to his former colleagues and students at the State Universities of New Jersey and West Virginia for aid and stimulating contacts which led to his work of correlation, experimental work on mouse cancer and to clinical friends.

A few acknowledgments follow, but I cannot hope to name a fraction of the people, men, women, boys, girls, and those peculiar individuals the college students, who have been my inspiration, comfort, and even arousers of the sympathy that spurred to more work through all these years.

After an excellent undergraduate training, with Biology and Chemistry under star teachers at Syracuse University, the writer studied with the greatest cytological neurologist that the world has ever seen, Dr. C. F. Hodge, Clark University.

Other work at the University of Chicago, with Professors in Zoology, Physiology and Anatomy, gave certain factual matter added interest, and stimulated my appreciation of the problems of applied Physiology of Development.

Like many another man, I acknowledge the help of Dr. Frank R. Lillie, of U. of Chicago, and the Marine Biological Laboratory. Dr. C. E. McClung of the U. of Penna. has also aided in many ways.

My sincere appreciation goes to Dr. A. M. Reese, to Prof. W. Hodge, and to "Chemical Sam" Morris, as well as many others at West Virginia University.

Since they cannot get at me, or even reply for a while, I'll state that I am greatly indebted to General Sir Robert McCarrison, of Oxford; Sir Arthur Keith, of Downe, Kent; Sir John Orr, of Rowett Institute, Aberdeen; the late Sir Frederick Banting, of Toronto, Canada, and the late Professor Poulsson, of Norway. Doing their bit for the Axis are Dr. W. Stepp, first in the World to recognize, in print, my development of McCarrison's principle of fat-thyroid-iodine

balance; and Dr. T. Ishihara of Takamatsu. Dr. Ishihara has used calcium with endocrine extracts in cancer at my suggestion.

The friendly interest of the Provincial Cancer Commission of Ontario, Canada, gave me an opportunity to talk to them in 1940. Experimental studies with spontaneous and implanted cancers were made possible at the University of Michigan, where the experience and kindly aid of that good friend to all the world, Dr. A. E. Woodward, proved of particular value. Members of the medical and scientific faculties were most helpful, and Professor G. R. LaRue with President A. G. Ruthven furnished every needed facility.

Through a national correspondence group with 50 clubs in the larger cities of some 30 states, the writer began, in the spring of 1933, the preparation of a series of reports on the chemistry of the endocrine glands and the role of nutrition in a variety of diseases, including cancer.

Three U. of Cincinnati men, the late President Herman Schneider, with whom I fought for iodine while he discussed specific wave-length radiation of elements in cancer and other diseases, Dr. A. P. Mathews, biochemist, and gentleman, and Dr. Shiro Tashiro, a real American, have all been of the greatest possible aid. So has Dr. Lawrence Wesson, for some time at Vanderbilt University.

But I cannot furnish the list of the Woods Hole people from 1907 on, so—;

At the Marine Biological Laboratory, Woods Hole, Mass., associates of some 30 years have been always ready to discuss chemical and physiological factors in growth, and by their keen criticism, forced greater clarity in the journal articles prepared by the writer on gland-nutrition-cancer relationships.

Substantial grants from two State Universities, the National Research Council, Sigma Xi, and the Purnell Fund, have enabled the writer to conduct experiments on both invertebrates and vertebrates which paved the way for his cleancut evaluation of iodine in the glands of internal secretion. Experiments on gland-vitamin relationships established certain principles regarding normal and abnormal growth, and the resorption of embryos.

The writer is especially indebted to the editors of foreign journals including the *British Lancet*, *Nature* and *Journal of Experimental*

Biology, and the *Belgian Archiv. int. de Pharmacodynamie et de Thérapie*, for extending contacts in Europe.

In the United States, the editorial of Dr. H. E. Howe in the *J. of Ind. and Eng. Chemistry* on our iodine work, and articles of my own published by *Int. Clinics*, *Medical Record*, *Medical Times*, *Medical World*, *Medical Searchlight*, and certain other scientific magazines have furthered friendly correspondence with general practitioners, and with research men.

Remarkable in its scope, the "Collecting Net" issued by still another brilliant Cattell editor, Ware Cattell, at Woods Hole, Mass., has aided in presenting my own theses with the keen criticism of friends who tolerate no nonsense.

Finally the loan library of the American Medical Association has made the author's reprints available to doctors since 1934.

Specific aid has been rendered by experts who have read sections of the MS, or who have discussed preliminary papers on cancer over a period of ten years.

My cousin, Adaline Eugenia Andross, my mother, the late Eugenia Stephens Chidester, and my wife, she who was Maud Cole Saxton, have kept my flame of hope, and the spirit of true consecrated Christian effort going—to the end. This is *their book*, too.

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"Such is my task. I go to gather this the sacred knowledge,
Here and there dispersed about the world, long lost, or never found."

—ROBERT BROWNING

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INTRODUCTION

Defeatism and Hope in Cancer

"'Tis time new hopes should animate the world,
New light should dawn from new revealings."

—ROBERT BROWNING

Today we have the finest organization in history to direct the public towards physicians early enough so that they may be healed. Yet, in cancer, that organization faces an almost insuperable obstacle.

For there is an atmosphere of defeatism, even among the experts. We are told by distinguished authorities that there is no hope for the prevention of cancer, and that all the efforts of the surgeons and the radiologists are able merely to remove individual cancers but not to cure cancer in a real sense. As a result of this pessimistic teaching, many persons delay in securing needed medical attention while others in whom cancer has developed have sunk into silence and despair.

It is not my province nor is it my desire to harrow the reader by repeating once more the statement made so often, that surgery and radiation are the only hope in cancer, and that they have failed. The "Cured Cancer Club" and hosts of people who have recovered from cancer show us that there is HOPE!

The widespread propaganda for early examination brought many patients to surgeons who have saved their lives for usefulness. Radiologists struggling with a weapon that is as potent as dynamite are recognized as slowly advancing in their knowledge of how to treat a limited group of cancers successfully. The road of progress in radiology is paved with the martyred dead who gave their lives to save their patients.

Among physicians it is natural that much real depression of spirit is felt because so many patients fail to seek their aid while there is a chance to remove the cancer completely before it spreads over the body. Moreover, it is true that relatively few persons survive after internal cancers have developed. It is difficult to determine from

the symptoms incipient cancers of the internal organs even if the patients did seek early aid.

The foremost authorities on cancer are working with all their energy to furnish suitable, safe adjuncts to the recognized treatments. The reason for repeated warnings about methods other than the orthodox, is the general disposition of the public to patronize quacks, and to indulge in dangerous self-medication. Just as fast as new aids in their healing art are developed the able clinicians apply them. But, they ask for clean-cut evidence first.

The public, knowing that friends have died shortly after they sought medical aid for cancer, cannot realize that these were far-advanced cases and would have died soon, without treatment.

The failure of modern methods in cancer is due in part however to a lack of knowledge regarding supportive treatment. Surgery and radiation will not in themselves furnish once more the body chemicals that cancers have either consumed or cause to be excreted in vast amounts. For the growth of a "parasite" like a cancer demands from the host essential foodstuffs and a chemical imbalance is set up which we may rightly compare with that induced by the growing embryo and fetus.

Such supportive and restorative treatment can best be given by a "family physician." We have departed too far from the custom of having an old friend of the family who functioned as medical advisor. Such a physician would not willingly permit a woman to let her goiter develop into a cancer of the thyroid. And he would not knowingly allow a nursing mother to run the risk of cancer of the breast, due to faulty care, after childbirth.

Every case of cancer should be treated by the general practitioner in conjunction with the specialist whose services, like his knowledge of individual cases, are perforce limited by short acquaintanceship. Far too many physicians specialize before they have had sufficient experience in general practice.

In his brochure for the American Society for the Control of Cancer, Dr. James Ewing says, "Because 95% of all established cancers are fatal, early diagnosis by the general practitioner becomes the most important weapon in the fight against the disease."

The "family doctor" knows the history of conditions that may predispose towards cancer in an individual, and a sympathetic physician will be sought early by women who might otherwise hesitate about securing careful examination for disturbed uterine function, or even for breast soreness. Bloodgood has said in a patient over 50 delay beyond one month may be fatal in some breast cancers.

It will be evident, as the reader proceeds, that the mystery regarding vitamin-gland relationships is involved in the fogginess that obscures some types of treatment. Vitamin deficiency causes glandular derangement, and glandular derangement and exhaustion pave the way for all old-age diseases including cancer. Thyroid cancer is one of the keys to the chemistry of cancer growth.

The case to be discussed now is one that a friend asked me to cite.

About thirty years ago, one of the finest of my friends married a lovely girl. To them was born a child. But that child suffered from the disordered thyroid gland of its mother and was hopelessly feeble-minded. Later the mother developed menopausal insanity, and finally died from cancers of the thyroid, ovaries, and intestines. Her thyroid gland, sub-normal in early years, became cancerous and spread by metastases to cause her death. Her two brothers also died from thyroid trouble.

This type of cancer is preventable and, if attacked early, is curable. Other cancers developed as metastases from thyroid malignancies include cancer of the lungs, breasts, brain, bones, ovaries, and intestines, and are likewise preventable. Shall we then say that knowledge of how cancers arise is lacking? It will be apparent as we proceed, that the chemistry of cancer growth involves tissue susceptibility, irritations, lack of blood supply, and inadequate nutrition. Wild-growths are not able to form unless proper local conditions favor them.

Certainly nothing could better promote the greatest happiness of the greatest number than a knowledge of the causes of those diseases that have increased so remarkably within the past twenty years.

"To know the cause of a disease is sometimes to be able to *cure*, often to be able to prevent it." This writer believes that the cause of cancer is to be found linked with the causes of other "old-age"

diseases which develop when the body chemistry is abnormal. Here, glandular function is at fault.

The late Doctor Francis Xavier Dercum of Philadelphia said in 1925, "What is the cause of the enormous increase in cancer in the modern world? To my mind, the cause is not far to seek. Never before in human history have the strains of life been more numerous, more incessant, and more severe. No wonder that nature cries out in revolt. No wonder that the group of glands upon which the expenditure of energy depends, the thyroid, the pituitary, and the adrenals, give way and that ordinary reparative processes can no longer be maintained; no wonder that their dependencies, the sex organs, fall by the wayside. This, I believe to be the story of malignancy. I believe this to be the cause of its increase."

The evidence published by Brown and Pearce of the Rockefeller Institute in 1923 is conclusive that normally *active glands of internal secretion* will protect rats against reinoculation with experimental cancer. Such glandular function also proved protective against animal infections with syphilis. Proper diets will aid in preserving the health of all glands.

One of the oldest theories of cancer is that of Cohnheim, who identified abnormal growths in different parts of the body with the pathological thyroid gland from which they originated. He advanced the hypothesis that cancer practically always arises from groups of *embryonic* cells that have become cut off during the development of the body, which retain their embryonic power of growth and which suddenly display this power. Undifferentiated embryonic epithelial masses are *rare* except in the glands of internal secretion.

Non-malignant or "benign" tumors have been classified as *lipomas*, which are fatty accumulations found on the back, shoulders, arms, or legs; *fibromas* of the skin; *myomas* of the muscles; *osteomas* of bones; *gliomas* of nerves; *angiomas* of capillaries; and similarly designated tumors of other parts. These may never become malignant.

The malignant growths include three chief types, *sarcomas*, which affect bones or glands; *carcinomas*, which may attack the breasts, liver, or intestines; and *epitheliomas*, which are found on the lips, mouth, nose, and eyes.

Certain cancers disseminate and give rise to a crop of nodules in parts of the body quite remote from their origin. The disseminated new growths are called *metastases*. They retain the structure of the primary tumor, thus we see thyroid tissue, readily recognizable both by microscopic and chemical tests, as tumors of the ovaries, bones, mammary glands, lungs, or brain. Carcinomas of the breast and the prostate gland quite commonly extend into the bones.

CHAPTER I

Cancer in Man and in Animals

DISTRIBUTION OF CANCER IN THE WORLD

"We are born to inquire after truth."

—MONTAIGNE

Cancer is found most commonly in the Temperate Zone. It is rare in primitive races where natural foods are eaten. In Ceylon, where the diet consists of oceanic fish and whole rice, the cancer rate is about 10 per 100,000 of population. In Greece, Italy, and Japan, where the foods are adequate in mineral constituents, the death rates in cancer are low. In Japan, this is directly correlated with the absence of goiter, and the use of marine fish as food.

In Denmark, where the foods are heavily salted, and strongly spiced, in 1928 the death rate from cancer was 1 in 5 among those over 45 years of age. It was well over 140 per 100,000 of population. In Switzerland, where cancer rates are almost as high as in Denmark, thyroid cancer is very common.

In the United States, cancer is second to heart diseases as a cause of death. The U. S. Public Health Report for May, 1940 lists the incidence of cancer in different states. The mortality for 1939 was 115.5 per 100,000 of population, for cancer. Diseases of the heart, many of which are associated with glandular malfunctions, were responsible for 277.1 deaths per 100,000 of population.

In 1939, South Carolina, called the "Iodine State," had the lowest death rate from cancer of all the states, registering at 54.2 per 100,000 of population. Other states where goiter is rare and where iodine is present in appreciable quantities in the soil and foods, also showed low cancer rates. On the other hand the states in the great "goiter belt" uniformly had high cancer incidence.

In his pamphlet on goiter in Switzerland, Dardel (1922) stressed the close relationship between goiter and cancer previously discussed

by Bayard. Dardel considered that goiter aids in promoting the genesis of cancer by inducing precocious senility and cell degeneration.

Remond, Sendrail and Lassalle (*C. R. Soc. de Biol.*, Oct. 30, 1925) showed that in rabbits in which experimental tar carcinoma had been induced, there was pronounced rise in the *basal metabolism* in the precancerous stages. Hyperthyroidism precedes gynecomastia, and male breast-cancers. (See page 118.) They cited investigations showing that endemic goiter predisposes to carcinoma. Koreschewsky, moreover, learned that *thyroidectomy* caused an increase in the growth and proliferation of neoplasms in dogs.

Wegelin, in his 1935 report on the autopsies in Berlin, Germany, as compared with Berne, Switzerland, has brought out strikingly the influence of goiter on the development of thyroid carcinoma. In Berlin, there were only 13 malignant thyroid tumors in 13,426 necropsies; but in Berne, where goiter *and* cancer are extremely common, there were 159 malignant thyroid cancers in 15,250 necropsies. (See D. Marine, *J. A. M. A.*, June 29, 1935.)

Tinker, of Ithaca, N. Y., who favors radio-cutting instead of incisions for biopsies, and whose technique in the *surgery* of malignant goiter is widely approved, has cited evidence on metastases from *apparently benign* goiters which caused death from cancer.

We know that Plaut (1933), Masson, (1933) and others have recorded numerous cases of ovarian cancers that were proved by pathological and chemical examination to contain thyroid tissue indicating their metastatic source.

In 1924, Stocks of London directed attention to the correlation between goiter and cancer incidence. The writer has, since 1933, emphasized the relationship between glandular exhaustion and the development of *all* the "old-age" diseases, including arteriosclerosis, cataracts, gallstones, and cancer. In Wales, Dr. W. Mitchell Stevens, for 30 years a clinician, has come to the same conclusion as this writer did from animal tests and from extensive survey of the literature and we have exchanged letters and reprints which show that, independently arrived at, our beliefs are similar, and in agreement with Stocks on cancer in goitrous regions. In April, 1939, McClen- don, the biochemist who brought out the fact several years ago that the Japanese have very low goiter incidence, published a report refer-

ring to the early statements of Stocks, and himself furnished evidence of goiter-cancer correlation, statistically.

Never before in the history of this country have we had so many cases of goiter. Glandular derangements are interrelated, and a thyroid cancer will migrate as metastases to the lungs, breasts, ovaries, bones, brain and internal organs. The same type of *chemical imbalance* which permits the development of thyroid cancer is seen in *other* cancers. For growth-acids (amino-acids and fatty acids) "unsaturated" sterols, and small amounts of the essential elements including iodine, will combine to cause growth acceleration. Moreover, these growth-acids are inactivated by the addition of proper amounts of iodine to them. (See pages 58, 95.)

In thyroid cancer the iodine present was not sufficient to prevent the goiter which appeared from becoming malignant. In other cancers, it has been proved experimentally that small amounts of iodine facilitate the growth of cancer cells, but that larger amounts will speedily inhibit growth. In fact the cancers that are *regressing* have been analyzed, and shown to have very high iodine-content. Holler, who discovered this in 1923, points out the increased affinity for iodine in tissues of low vitality.

The fact that all glands of internal secretion are iodine-reservoirs, and the relationship between iodine and the inactivation of growth substances in cancers, have been brought out by this writer since 1933 in the series of medical and scientific articles placed in the loan library of the American Medical Association. Other significant relationships include the rôle of the vitamin-rich foods as sources of needed balancers and normalizers of the glands of internal secretion, and the action of iodine, iron, and calcium as defensive agents against injury by radiant energy. These are all by way of support for the conclusion that *natural foods* with adequate minerals and vitamins will protect against cancer because they aid in keeping the glands of defense up to normal function.

"I have made life consist of one idea;
Ere that was master, up till that was born,
I bear a memory of a pleasant life,
Whose small events I treasure."

—BROWNING

OCCURRENCE OF CANCER IN ANIMALS

One of the first instances of cancer to be linked with diet was the thyroid cancer that developed in trout in the hatchery ponds of western New York State, more than thirty years ago. The fish had been fed on pig liver, which has considerable fatty material in it. Later investigations by Walter Hess have shown that such a diet causes serious derangement of the liver and pancreas in the trout of that same region. Marine fishes are known to develop cancer. This would seem to be an argument that our dietary adjuncts of marine fish may not protect against cancer. But it is merely an instance of the power that certain cancer-producing factors have, to over-rule protective substances. For fish live, struggle against vicissitudes, grow "old" and succumb to diseases.

The common frog and toad are used in growth studies, and spontaneously appearing cancers in the frog have been studied for several years by B. Lucké of the University of Pennsylvania. He emphasized in his 1940 report the fact that in the frog malignancies are not dissimilar in structure from normal tissues, and their method of growth is in definite, well defined patterns. Thus they are not "wild-growths." Tissues from amphibia were used in the pioneer research of R. G. Harrison more than 35 years ago, when he developed a technique for studying the growth of nerve cells and associated fibers, in "tissue culture." Remarkable research by Alexis Carrel, Montrose Burrows, the Lewises, and the group at the Strangeways Laboratories, London, has followed. In studying tissue cultures of chick muscle-cancer, Sato has used iodine in small amounts to accelerate such growth. McCarrison has used glands themselves in tissue cultures, and regulated their growth by different amounts of iodine.

The *fowl* has been used a great deal in cancer research since the remarkable investigations of Peyton Rous brought out the value of his chick-tumor, transplanted by a filterable substance, first classed as a virus. Tissue cultures of chick embryos are much used in experimental cancer. Other birds which develop cancer in nature include the canary, the parakeet, the goose, and the turkey.

Cattle, sheep, pigs, dogs, cats, rabbits, guinea-pigs, rats and mice have all been shown to develop cancer. Tumors in the horse have been treated with iodine for many years past, by veterinarians.

The earlier work with rabbits has been largely replaced by studies with rats and mice. Dr. Maude Slye of Chicago has studied heredity in mouse cancer more than 30 years. Dr. C. C. Little of the Jackson Memorial Laboratory has built up a large colony of cancerous mice, which are available for research purposes.

HISTORY OF CANCER

The first written record of cancer is found in the Ebers papyrus, dating back to 1500 B.C. Old Indian and Persian writings mention it. Herodotus, a Greek, known as the "Father of History," describes a cure of breast cancer in 600 B.C.

An early statuette showed a woman with an ulcerating cancer of the breast. Hippocrates invented the term *carcinoma*, to indicate a malignant tumor.

Galen, who lived 129–201 A.D., prepared a classification of tumors that was used for 1500 years. He considered that cancer was caused by an excess of "black bile."

The first complete authoritative study of the microscopic appearance of diseased tissues was that of Johannes Müller issued in 1838. Virchow developed the cellular theory of disease and fathered the idea of removing portions of a cancer for further study, known as *biopsy*.

For many centuries there was close adherence to the belief, stated by Hippocrates, that "deep seated, non-ulcerating cancers did better without such treatment as was then available."

In the 17th century Fabricius Hildanus (1560–1624 A.D.) was first to follow removal of the breast by the radical procedure of dissecting out the lymph nodes of the axilla. This method is still considered safer than extensive radiations by many surgeons.

Paré (1509–1590) suggested that a "cancer is a hard tumor spread abroad to the similitude of the stretched out legs of a crab." He therefore by his appended drawing of the crab, CANCER, gave us the term now in use.

Le Dran (1685–1770) of France and John Hunter (1728–1793) of England recognized that cancer was a local disease in its early stages and that it spread through the lymphatics to the lymph nodes and thence to other organs. Recamier, in 1829, described the inva-

sion of fragments of cancers into veins, and first used the term metastasis (transfer to a new place).

The first experimental transplantation of tumors in animals was done by Hanau, of the University of Zurich, in 1889. He was so depressed by the apathy with which this remarkable contribution was received, that he committed suicide.

The first tissue culture work was done by Leo Loeb, who reported in an article printed privately, in 1897, his experiments on cultures in vitro. He later described his work more fully in *Roux's Archiv. Entw.* in 1901. Fetal epithelium of the guinea pig was cultivated in agar and coagulated blood serum.

Carrel and Burrows, in 1911, adopting the tissue culture technique of Ross G. Harrison, grew small bits of tumors in glass flasks.

In 1914, Fibiger of Copenhagen reported that he had induced tumors in the stomach of rats by feeding them cockroaches that were infested with parasitic worms. His experimental procedure followed accidental observation of adult roundworms in rat-tumors. He then traced the Nematodes to their secondary host, the cockroach, and fed cockroaches to other rats with the result that they developed tumors.

In 1916, Yamagiwa and Ichikawa announced their discovery that by painting the ears of rabbits with coal tar for a long period of time, tar-cancer developed. For several years the Buffalo State Cancer Hospital group have been able to cause cancer in experimental animals by *feeding* tar.

The application of X-rays to the treatment of cancer by Sjögren, in 1899, paved the way for a vast amount of experimental work with radiant energy. For Sjögren cured a case of carcinoma of the cheek thus. In 1898, the discovery of radium by the Curies stimulated the use of that powerful substance. In 1903, two cases of facial cancer were treated successfully by Goldberg and London, using radium. The value and the great hazards incident to the use of radiant energy are discussed by us on pages 144-146.

Continued use of X-rays, like the repeated application of coal tar to animals, will have general systemic effects not considered sufficiently in analyses of results obtained on the defense mechanisms. In animals that have received coal-tar applications on the skin, the lymphoid organs and the liver show changes comparable to those

induced by a generalized exposure to X-rays. Cramer has shown that such X-ray exposure may be compared to *vitamin deficiency* in its influence on rats. The injection of the active hydrocarbons of coal tar into young immature animals tends to stunt their growth and thus indicates definitely an action on the glands of internal secretion, especially the thyroid gland. It fits into our own conception of stimulation and exhaustion. (See page 102.)

Inheritance of mouse cancer, first studied by Tyzzer in 1907, and extensively investigated since 1908 by Professor Maude Slye of the Sprague Memorial Laboratories, University of Chicago, has attracted the attention of other able authorities on heredity, including especially the group headed by Director C. C. Little of the Jackson Memorial Laboratory, Bar Harbor, Maine. Today, we have available for experimental work racial lines of mice that are known to have extremely high cancer incidence. With them, research students have been able to develop for comparison lines in which resistance to cancer is notably high.

The successful implantation of a number of tumors has been secured in rabbits, rats and mice, and these animals are also available with their special new-growths for experimental purposes.

The common method of producing tar-cancer in rodents has been augmented by the application of other cancer inducing agents, such as derivatives of the shale-oils and of coal tar hydrocarbons. A vast literature has grown up dealing with results obtained by such tests, and with cancer destroying substances.

Experimentally, by using some agent, malignancy has been produced in animals in skin, connective tissue, muscle, bone, bone marrow, lymphoid cells, lungs, stomach, gall bladder, liver, testis, mammary gland, the uterus, and other tissues. But the actual transformation of normal cells to malignant ones has not been witnessed. The new-growth of malignant cells is not distinguishable in its origin from normal growths. It seems that most cells may be rendered malignant by the action of one or more agents.

There is always a question about the implanted cancers, for in some animals they regress rapidly after a short period of growth. This apparently "spontaneous" cure of inoculated cancer is undoubtedly due to the action of *bodily defense mechanisms*. Burrows has

shown how, by vitamin therapy, it is possible to hasten such regressions when oil-tumors or X-ray tumors have developed. Probably the best evidence that we have in this connection is the 1923 report of Brown and Pearce (Rockefeller Institute) that in rodents with the *most active* set of glands of internal secretion, there proved to be the *greatest resistance* to inoculations with experimental tumors.

In line with our own conception of bodily defense, the recent report by Bittner is in point. When the offspring of cancerous mice were nursed by foster-mothers of a non-cancerous strain, they showed a 96% lower incidence of cancer than their litter-mates. If this finding is as significant as it appears, we shall proceed shortly to a chemical knowledge of cancer resistance not generally believed possible. The logical development of such work is the test of chemically altering the secretions in the cancer-susceptible mother. Naturally, the writer is inclined to the belief that iodine added to the diet of nursing mice of cancerous strains will reduce their tendency to transmit cancer through the milk. The addition of *iodine* to the *milk* of such cancerous mice might also inactivate the cancer producing factor. It is highly probable that their colostrum for the first few days will be rich enough in iodine to be protective also.

This writer has experimented with problems of growth during the nursing period, and the *prenatal development* of vitamin and glandular deficiencies in rodents since 1912, and hopes to attack the problem of regulating prenatal susceptibility and resistance to cancer.

HUMAN-CANCER TRANSPLANTS INTO ANIMALS

Towards the end of the eighteenth century, a French scientist, Dr. B. Peyrilhe, attempted to inoculate dogs with human cancers, but was unsuccessful. Others have from time to time made similar tests, but with no success. Presumably many such tests have never been reported.

In 1938, Dr. Harry Greene of the Rockefeller Institute reported that he had succeeded in transplanting breast cancer from a woman to the eye of the rabbit. (*Science*, October 24, 1938.)

Steiner has reported (1940) successful production of sarcomas in mice, by injection of extracts from the livers of persons who died of cancer.

The livers were ground and preserved in an equal amount of 95% alcohol. Then they were saponified with alcoholic potassium hydroxide (KOH) for 24 hours in a steam bath, water equal to the amount of alcohol in the mixture being added. Further treatment with ethylene dichloride, evaporation, and final dissolving in sesame oil preceded the tests. The sesame oil was tested repeatedly and showed no cancer-inducing properties, either unheated, or after heating.

Injections of about $\frac{1}{2}$ gram of the extract, in .5 cubic centimeter of sesame oil into each of 56 mice, was effected subcutaneously, on June 1, 1939. The first tumor appeared between 5 and 6 months after injection. The mouse died, 182 days after injection, with a large tumor measuring 33 x 25 x 22 millimeters. At the end of 16 months, Steiner reported that of the original 56 mice injected, 37 were living. Thirteen tumors had appeared, and 7 mice showed no visible tumors.

The livers were taken from 8 cases of human cancer, of which there were 2 carcinomas of the lung; 3 carcinomas of the stomach; and 1 case each of cancer of the esophagus, pancreas and rectum. No carcinomas were found in the livers of these patients. This is of course not an instance of transmission of a human cancer itself to an animal. (Steiner, Paul E., *Science*, 92, No. 2393, Nov. 8, 1940, pp. 431-432.) Steiner has further reported (1943) that after injecting *mice* with a substance extracted from the urine of *human* cancer patients, cancer developed. The carcinogenic substance is described as an unsaponifiable lipoid.

DANGER SIGNALS IN CANCER

"Cancer never appears spontaneously in uninjured tissue."

—BILLROTH

Skin

Cancer of the skin is most common in old persons, but may occasionally appear in children. A sore on any part of the body, which does not heal, or a rapidly increasing growth in a wart or a mole should be examined at once by a capable cancer expert. Cancers of the skin have been treated by radiation methods for many years,

because they were so accessible. Nevertheless, a pigmented mole should always be excised by surgery, as it metastasizes early.

Bone

Cancer of the bone is found in young children as early as 8 months. The legs of *boys* are most often involved, but any bones may be affected. Bone cancers grow rapidly, and the pain is intense. But in early stages, cancers of the bones are mistaken for sprains or even rheumatism.

Irradiation has made little headway in malignant cancers of the bone. Surgery is valuable, but it must be remembered that distant metastases spread rapidly.

Lip

The danger sign of lip cancer is a slight sore that does not heal. Lip cancer spreads rapidly, and should be attacked early. Surgery and irradiation are successful in many cases. Irritation is a common cause in smokers. Fishermen sometimes get tar-cancer from their tarred nets.

Mouth

Cancer of the mouth, especially that of the tongue, is five times as common in men as in women. It frequently appears, between the ages of 40 and 60, in persons whose teeth or poorly fitting dental plate produced an irritation, and a small ulcer. Sometimes a white spot appears. The rapid spread of mouth cancer makes it necessary that early treatment be given.

Stomach

The most common form of cancer is cancer of the stomach. After the age of 40, lack of appetite for meats, obstinate indigestion, colicky pains in the stomach, and loss of weight may be an indication. But, unfortunately in many cases pain is not present.

Alvarez has cited two cases to illustrate this point. The mother, a gentle old lady with a cancer of the stomach, maintained that she was not suffering, and needed no treatment. But she was greatly concerned over the health of her daughter who for three weeks had

been vomiting everything she had eaten. What was the matter? Nothing but *fear*. The daughter became ill the moment she heard the mother's trouble.

It should be noted that dietary deficiency, alcoholism, and worry, all cause gastric ulcers, and that eventually malignant growths may develop. (See pages 37, 77.)

Dr. W. A. Cooper, discussing the problem of gastric cancer (*J. A. M. A.*, 116, pp. 2125-2129, May 10, 1941), states that the despondent outlook of physicians toward cancer of the stomach is justified only by the high proportion of failures in the past (95%).

New York Hospital experience indicates that operable cancer of the stomach is cured in 44.4% of cases for a period of 5 years by gastric resection, a result comparable to breast cancer results. This is most encouraging for breast cancer is generally regarded as curable if operated on in time.

Alvarez of the Mayo Clinic has reviewed the study of 10,000 cases of cancer of the stomach prepared by Drs. Waitman Walters, H. E. Gray, and J. T. Priestley, from cases treated at the Mayos from 1907 to 1938.

Alvarez points out that 24% of all patients operated on recovered completely. In those who were operated on early, the percentage of cures rose to 60%. He urges that patients with the following list of symptoms seek their physicians at once. Indigestion, loss of weight, vomiting, pain in the pit of the stomach.

Intestines

Intestinal cancer is found most frequently in older groups, from 60 to 70 years of age, but it may appear in young persons or even *children*.* Alternation between diarrhea and constipation, pains in the abdomen, the passage of slime, and ultimately the passage of blood in the stools indicate cancerous condition. Surgery is the proper treatment. It is claimed by some that radiation is also beneficial, but other authorities state that "in carcinomas of the esophagus, stom-

* Bacon, Wolfe and Archambault of Philadelphia reported two cases of malignant rectal tumors in boys aged 3 years, 8 months; and 4 years, 7 months, respectively. They cited other cases in children from the literature. (*Am. J. Dis. Child.*, 64, July, 1942.)

ach, rectum, liver and pancreas, little headway has been made by radiation."

Uterus

Cancer of the uterus is the most common form in women. It develops in the age group between 40 and 50 years, at the menopause. Pain is not present at the beginning, and since the signs of bleeding may be ignored by the patient, as not significant, early diagnosis is often not possible. Excessive menstrual flow, bleeding after the menopause, and bleeding between the menstrual periods are cited as danger signals. Surgery and radiation are both recommended by able cancer men.

Breast

Mammary cancer is common in women. It is more frequent in women who have not nursed babies,† than those who have, and it is commonest in single women. The danger signal is a small lump in the breast, usually painless. In women over 40 such a lump should be removed at once, for delays are dangerous. Surgery is the most effective method. Pre-operative radiation is advised by some clinicians, but others frown upon it, and upon any radiation of such cancers. Complete operative excision of axillary lymph glands should accompany such an operation, for safety.

The foregoing will serve to emphasize some of the more common types of cancer, and their warning signs, if any.

"Men fight best if rightly afraid."

—HALL

DIAGNOSTIC TESTS FOR EARLY CANCER

A universal diagnostic test for cancer has been long sought. For many cases of cancer come to the surgeon in a hopelessly advanced stage, with abundant metastases, and with greatly lowered bodily resistance.

† When a mother fails to nurse her baby, she robs the child of its most valuable natural food. And she runs the risk of mastitis, and of breast-cancer, due to the decay of residual, unexpressed milk.

It is evident at once that a disease which has been compared to pregnancy in its action on the body of the host will cause certain chemical changes in the body fluids. That such changes can be *specifically* identified as due to cancer, is another matter. In general, experts disbelieve claims that are made for specific cancer-tests.

Botelho's Nitric Acid-Iodine Test

Botelho, in Paris, announced about 1920 that he had developed a chemical test for cancer. E. F. Smith, in his article on cancer in *Science*, June 12, 1925, described the method, and also stated that a Japanese, Dr. Ichikawa, confirmed Botelho's findings by tests with rabbits that had developed tar-cancer.

Botelho adds dilute nitric acid, plus an iodine reagent, to the blood of the suspected case. First he standardizes the blood to a specific gravity of 8% albumen, and centrifuges it. Then the reagents are added in several small doses, with the test tube shaken after each addition. The normal serum remains clear, but the serum of cancer patients remains persistently clouded.

Schiller's Iodine Test for Cancer

The iodine test of Walter Schiller, as described in *International Clinics*, 4, 1934, is based on the fact that cancerous tissue has a higher sugar metabolism than normal tissue. Warburg has shown that tumor tissue by glycolysis produces its own weight of lactic acid every eight hours, in one of the rat carcinomas. Carbohydrates such as dextrose, or glycogen, will break down into lactic acid. In normal tissues, lactic acid can be reconverted, or destroyed, but in cancerous tissues, it remains as an irritant, and aids in the growth and dispersal of the cancerous growth. (See pages 60-62.)

Glycogen, which is stained dark brown, by iodine, is present in some living tissues, but is ordinarily absent in cancers.

With Schiller's test, a pledget of cotton, dripping in Lugol's solution of iodine, is applied to the mouth of the womb. Normal tissues take on a deep chestnut brown color (due to glycogen) but cancerous tissues remain unstained, or take on a pale yellow color.

Martzloff of Portland, Oregon, and Galloway, of Evanston, Illinois, have both attested to the value of Schiller's test, when used to

determine the loss of glycogen that is characteristic of the mucous covering at the mouth of the uterus in cancer of that region.

Schiller's test is inapplicable to all cancers since it is a local one.

Spectroscopic Differences in Blood of Cancer Patients

Dr. Burton Hyde of Ohio has furnished us with a significant report on his use of irradiated blood from a patient, which is treated, and then reinjected intravenously. (See page 154.)

As a result of his spectroscopic comparisons, Dr. Hyde, aided by his associate, the spectroscopist, Professor Wendell Koch, has presented evidence that the blood of cancer patients differs from that of normal persons. He says—"From the clinical side, and from experiments on human blood, I think that there is a definite chemical condition which is a prerequisite to the development of cancer. Cancer can only get its food supply from the blood, and the active condition can only be carried by the blood. Therefore the blood should show some characteristics not present in other diseases."

The absorption spectrum of the blood of cancerous patients was shown by Hyde and Koch to be transparent to the ultraviolet region, after irradiation. They attribute the condition to the flocculation or precipitation of some constituent which absorbs ultraviolet radiations. In the normal blood there is no such precipitate to bring the coloring matter (hemoglobin) with it. They were able to distinguish between the appearance of the blood of tuberculosis afflicted cases and that of cancer patients, although the tubercular individuals also showed a deviation from normal in the tendency towards transparency to ultraviolet.

Since this is really in part a hemoglobin test, we should like to see records of anemias. As a matter of fact an *anemic* condition develops in cancer patients.

Other Types of Blood Diagnosis

The Freund-Kaminer test was based on their discovery that the blood serum of non-cancer patients destroys cancer cells, while in cancer patients the serum has no such ability.

The Fuchs test is based on his claim that the blood from cancer cases will digest heated fibrin, but that normal blood lacks this quality.

Robinson has used this test at Vanderbilt University with 200 patients; Rosenthal at the University of Pennsylvania.

Pfeiffer's crystallization test (1938) is carried out by studying the crystals formed after dilute copper chloride has been added to distilled water plus the blood under consideration. A "wing pattern" of crystals indicates cancer. The Pfeiffer crystals appear when saliva, urine and skin secretions (as well as blood) are added to cupric chloride. Dr. O. C. Gruner of the Archibald Cancer Research staff at McGill University has done extensive work with the Pfeiffer method. In 122 proven cases of cancer, Gruner secured (with polarized light) readings of 90% correctness.

It is worthy of note that in gallstone disease, where the patterns resemble "cancer patterns," *high cholesterol* is found in the blood as it is in cancer. We have already discussed the significance of cholesterol and cancer growth. (See pages 8, 98, 101, 109.)

Other blood tests have been reported favorable by Brossa, Bohne, von Dungern, and Abderhalden.

Sulphydryl-Inhibiting Effect

In 1937, E. Waldschmidt-Leitz announced that for some two years he had been testing the action of the blood serum from cancer patients on certain partially activated or inactivated substances. The lower activating power in cancerous serum indicated a deficiency in sulphydryl activity, he believed. He termed it a sulphydryl-inhibiting effect. Sulphydryl, so named from its content of sulphur and hydrogen (SH), consists of certain amino-acids that have been identified recently by Voegtlin and others with cancer research. The variation in *sulphydryl* in the blood is dependent in part on the action of the thyroid gland. Oxidations are aided by the presence of iron, and iron distribution is also linked with the proper functioning of some of the glands of internal secretion. It is also related to calcium distribution, for as we have pointed out, W. G. MacCallum has shown that *iron* and *calcium* are laid down in the same bony storehouses.

The tests have been made with several hundred cases, it is claimed, and of these "there was only about 5% error." The specificity is urged because benign tumors do not cause the loss of normal activating power, in the blood.

Cancer Serum Causes Pregnant Rabbits to Abort

In 1939, at the New York University Medical School, Dr. G. B. Wallace, and Dr. T. H. Elsasser announced that they had demonstrated that the urine or the serum of cancer patients, injected into the veins of pregnant rabbits, caused them to abort their young in 5 days time.

Elsasser and Wallace, in 1937, were making tests with the urine of patients, to induce the pregnancy reaction of Aschheim and Zondek. In this test, the urine of a pregnant animal is injected into a virgin female mouse and causes the ovaries to swell and also induces specific changes in the secretions of the reproductive organs, which are detected by vaginal smears. In some instances, the pregnancy reaction has been obtained from *male* urine. Especial interest was first aroused by a case which was that of a man who had *cancer*. Virgin animals show stimulation of the sex glands, but the startling effect of the cancer serum and urine was to cause abortion in pregnant rabbits.

The fact that a cancer is "like a baby" and stimulates the glands of internal secretion greatly, by its demand for essential foods, has been brought out by us, elsewhere. (See page 16.) And, we have shown (Chidester, *Med. Rec.*, June, 1934) how the ability to cause prematurity, exhibited by pregnancy urine, is also seen with glandular extracts, and with iodine. Moreover, iodine released in large amounts under stress and strain of emotions, we have identified with miscarriage. (See Chidester, *Med. Rec.*, 1934; *J. of Med. Practice*, 1936.)

Pregnancy urine or serum will act by virtue of its effect on the glands that control iodine, we believe. The reaction known as a pregnancy test occurs in cases where we know of profound glandular activity and excessive iodine in the excretions as in menstruating women. There are a number of diseases that confuse the results in such tests. Moreover, several endocrinologists about whose masculinity there can be no question have been able to use *their own urine* and secure typical pregnancy tests in animals.

Failure of tests with the "female sex hormone" and the anterior pituitary may mean *quantitative* difference in the chemicals that are present in the agents.

In view of the fact that the urine of normal men will sometimes cause the pregnancy reaction to appear in experimental animals, the striking studies of J. O. Ely are in point. Ely repeated successfully the experiments of Elsasser and Wallace with the urine of cancerous patients, and he also caused the reabsorption of embryonic rats by injecting the urine of a normal, healthy man.

Essenson in 1933 (*Medical Journal and Record*, 137, 11, 451-) said, "I used adrenalin as the confirmatory test in early pregnancy before the Aschheim-Zondek test, or the Friedman test became known."

As we pointed out in the same journal in 1934, the test for *thyroid* overactivity known as the "Goettsch test," is the *adrenal* test. Moreover, Sümegi has identified cancer with an overactive thyroid. (See page 168.)

The fact that after cancer has developed, the glandular mechanism persists in its attempts to mobilize cancer-destroying elements, identifies the tumorous growth still further with the body chemistry of pregnancy. For in each case a *parasite*, demanding foods, causes glandular stimulation. The growing cancer demands an inordinate amount of iodine from a host that has already undergone devastating attacks on its protective mechanisms.

To identify cancer after tests with urine or serum which may be duplicated with preparations from perfectly normal sources, is as uncertain as it is to adhere firmly to a *pregnancy test* that may be given by the use of urine from normal virgin menstruating women, or healthy, virile men.

Antiserum from Rabbits

In the July, 1940 issue of the *American Journal of Cancer*, Welker and Mann announced satisfactory tests with a new serum from the blood of rabbits. Aluminum hydroxide containing ground and specially treated *cancer tissue* is injected into rabbits and causes the mobilization of defensive antibodies in the rabbits' blood. The new serum is said to be specific for *cancer proteins* and not to react with normal tissues, or the blood of normal patients.

The serum gave positive results with a very high percentage of cancer cases. In the tests of cancer of the uterus (womb) the posi-

tive reactions were 87%, seven positive reactions in eight cases tested.

Dr. Welker in transmitting a report to "Science Service," expressed the hope that the report would not have the "cruel" effect of raising false hopes in laymen. Diagnosis and even *treatment* of cancer by the antiserum have been suggested, but *not* by Drs. Welker and Mann.

This writer agrees with Dr. James Ewing in his statement that "there is no rational basis for the hope that any test for early cancer will ever be found."

TEN GOLDEN RULES OF THE CANCER EXAMINATION *

1. Examine the lips, tongue, cheeks, tonsils, and pharynx for persistent ulcerations, the larynx for hoarseness and the lungs for persistent cough.

2. Examine the skin of the face, body, and extremities for scaly, bleeding warts, black moles and unhealed scars.

3. Examine every woman's breast for lumps or bleeding nipples.

4. Examine the subcutaneous tissues for lumps on the arms, legs, or body.

5. Investigate any symptoms of persistent indigestion or difficulty in swallowing. Palpate the abdomen.

6. Examine the lymphode system for enlargement of the nodes of the neck, axilla, or groin.

7. Examine the uterus for enlargement, lacerations, bleeding, or new growth. Make a bimanual examination to determine the condition of the ovaries.

8. Examine the rectum, and determine the cause of any bleeding or pain.

9. Examine the urine microscopically for blood.

10. Examine the bones and roentgenograph any bone which is the seat of a boring pain, worse at night.

Frank E. Adair, M.D., in *Southern Medicine & Surgery*, August, 1937.

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CHAPTER II

Heredity

From her remarkable study of the past 30 years on the inheritance of cancer in mice, Dr. Maude Slye of the Otho Sprague Memorial Institute at the University of Chicago, has shown that certain lines develop specific types of cancer. Her investigations of more than 140,000 mice show clearly the great variation in susceptibility of some races of mice to the development of cancer.

Dr. Slye's evidence shows how predispositions toward cancer will determine whether experimental mice will respond to irritations, or not. For example, in a strain of mice susceptible to lip cancers, she filed down the teeth so that they could no longer irritate the lips, and cancers of the lip did not develop in animals thus protected. In other lines, resistant to lip cancer, the irritation that sufficed to induce cancer in the susceptibles had no such effect and cancer did not appear.

Warthin has reported an interesting family in which three smoking brothers developed lip cancer much earlier than their non-smoking brother. Smoking is responsible for a great increase in lung cancer, statisticians tell us.

HUMAN CANCER FAMILIES

In an extensive study of 6000 cancer patients including their family histories made from 1908 to 1934 in Norway, evidence shows that hereditary disposition is a significant factor in the origin of human cancer. And heredity also determines the localization of the cancers, as in Dr. Slye's mice.

Dr. M. Macklin of London, Canada, has made important contributions to the statistical evidence on cancer, and has shown how frequently several members of a family are known to develop the same type of cancer in the same place, at about the same age. Occasionally, however, even in twins there may be some difference in the time

of appearance of the lesions. Phillips, at the Mayo Clinic, described such a condition in 1938. In twin women, the first twin, who had no children, developed cancer of the breast three years before her sister, a woman with 2 children. The relationship between glandular function and breast cancer will be discussed soon. (See page 118.)

The Bonaparte family constitutes a historically noted group in which there was a tendency towards cancer of the stomach. The father, Carlo Bonaparte, died from cancer of the stomach at the early age of 39. His wife did not die from cancer but, of their five sons and three daughters, two of the sons and two of the daughters are recorded as dying also from cancer of the stomach. Napoleon, who had suffered from severe gastric upsets for 5 years, was finally exiled at Elba, and died at St. Helena seven years later, in 1821. Historians relate that Napoleon was ill just before several of his military failures. He told his doctor that the physicians of Montpellier had stated that cancer of the stomach was hereditary in his family.

A family, about which we know more with reference to the development of cancer in its members, was reported first by Dr. A. S. Warthin in 1913. Later he gave another report in 1925, and after his death his colleagues at the University of Michigan, Hauser and Weller, gave a further account of cancer incidence, bringing the records up to 1936.

The father who founded this line died in 1856 at the age of 60 with cancer of the stomach. The average age at which cancer was diagnosed in descendants, or at which cancer had occurred, was 48 years. Only one of the descendants of this paternal founder developed cancer at 25 years of age. Of the ten children of the founder, 6 of them (4 sons and 2 daughters) had cancer. This gave an incidence of 60% in the second generation. Of the 4 cancerous sons one had nine children of whom 6 developed cancer. Another son had eleven children two of whom developed cancer. Of the 54 deceased members of this family who reached the minimum cancer age of 25 years, 35 or 64.81% developed cancer.

Of the 305 descendants of the cancerous founder of this family, 174 attained the age of 25 years, and of this number 41 developed cancer. Forty-three primary cancers occurred in the 41 individuals, and of these 26 appeared in the gastro-intestinal tract. Thus there

was exhibited a remarkable organ susceptibility. Forty-two of the growths were of the same type, adenocarcinomas.

Wood and Darling (*J. Cancer Research*, 1943) have described a cancer family in which females of four generations nursed by their mothers developed cancer of the breast. In another family five sisters were similarly affected. Transmission of cancer by nursing has been demonstrated in mice by Bittner. This is *not* hereditary.

CHEMICAL FACTORS MODIFYING HEREDITY

Besides the hereditary factors there are certain chemical substances which are controlled by the organs of internal secretion. The interrelation between breast cancer and the ovaries has been experimentally brought out by Leo Loeb and others, for mice from lines where breast cancers regularly appear were shown to be freed from susceptibility to it if they were subjected at an early age to complete removal of the ovaries. The recent studies of Wooley make it necessary to modify our conclusions on this finding. (See pages 192 and 193.)

Experimentally, cancer of the breast has been produced in male mice by injecting a glandular extract, and even by a synthetic product, of similar chemical constitution. We know that human breast cancers may appear after an abnormal enlargement of the male breasts, which had been preceded by thyroid overactivity. There is an intimate relationship between the thyroid gland, the sex glands, and the mammalian breasts. (See page 225.)

When we realize that the control of cholesterol and the development of the mammalian brain are determined in embryos by the activity of certain glands, especially the thyroid, and that failure to develop normally is associated with various diseases in the mother that influence the glands of internal secretion, it is not a far cry to the conclusion that inheritance of a *tendency* towards cancer in a certain region of the body may be linked with glandular function.

Dye has shown that removal of the thyroid gland in young dogs causes abnormal growth of the skull. Stockard has been able to produce some very peculiar dogs, hybridized between several divergent types. The glandular function that determines a rapidly maturing, very small Pekinese, indicating thyroid activity, is quite different from

that apparently involving the pituitary gland, which is responsible for the growth of such large types as St. Bernards and mastiffs.

We know that abnormal overactivity of the glands controlling calcium may be corrected in women who are losing large amounts of calcium during pregnancy by removal of the ovaries. And this same operation has proved successful in experimental animals and in some human cases in preventing and, certain surgeons claim, in *curing* cancer of the breast. Few clinicians now resort to the operation since its value is doubtful.

Ovariectomy is a truly terrible operation for it causes profound glandular upsets. A sterilized woman must take extracts, and her craving for maternity may cause profound mental anguish, with serious effects on her general health. Thus, resistance to disease is lowered. Some substitutive "sex hormones" are cancer-inducing we are warned by experimentalists and clinicians.

Thyroid gland therapy is beneficial in diseases involving the excessive losses of calcium. It has been used also in the successful treatment of breast cancer. (See pages 169 and 170.)

If inherited glandular makeup is responsible for various types of growth, why cannot we consider that it is related to the susceptibility of certain regions to cancer? Thyroid feeding influences breast growth; an overactive thyroid in men may pave the way for breast cancer. Vitamins which tend to normalize the glands of internal secretion will increase resistance to the development of cancer. (See pages 73-108.)

AGING AND CANCER

Syphilis is known to hasten the development of cancer of various types. Musgrave Woodman has said, "When the soil has been damaged by years of absorption of alcohol, or has been affected by syphilis, or even impoverished in its arterial supply by arteriosclerosis, it easily undergoes necrosis." This indicates two things, the influence of premature aging of tissues on the incidence of cancer and the rôle of syphilis in the accomplishment of such a condition.

Syphilis causes profound derangement of the glands of internal secretion, so that when prematurely exhausted they cannot prevent arteriosclerosis, or the other instances of accumulation of excessive

amounts of cholesterol characteristic of old age. Since cholesterol is an important constituent of the most malignant cancers, it can be seen that our explanation for the hereditary tendency towards cancer resolves itself into a matter of easily weakened glands. We know how great a difference exists in families with reference to their susceptibility to goiter and to diabetes. Goiter may lead to cancer of the thyroid, and thyroid cancers are known to metastasize to the lungs, breasts, bones, brain, and internal organs. That thyroid cancers readily migrate to the ovaries has elsewhere been brought out. (See page 188.)

Deranged sugar metabolism is linked with abnormal functioning of the thyroid as well as the pancreas. Preliminary over-activity of the thyroid is known to be related to cancer development, and diabetes has been suggested as a possible indicator of glandular derangement, which paves the way for cancer, by Dr. Shirlaw. Shirlaw kept records of his patients for years and found that some, with an early history of excessive sugar in the blood and urine, later developed cancer. (See page 183.) Records of body chemistry in cancer patients are woefully lacking and it is because of this fact that spectacular "diagnostic tests" have attracted attention to conditions in the body fluids that are common to *several* diseases where defensive organs are *active*.

Cancer has long been termed an "old age" disease, and it has lately been recognized that by protection against death from contagious diseases in youth we now increase the number of persons who live so long that they develop heart disease, arteriosclerosis and cancer. It is interesting to note that Mumford in 1936 reported twins in whom cancer of the breasts developed at about the same time, when they were 91 years of age. If they inherited a tendency towards cancer, it surely was slow in developing.

Madge Macklin in an address to the American Association for Cancer Research said, "Even though the manner of inheritance could be learned for every kind of cancer, it would be impossible to breed it out of the human race because of the age at which it develops. Since practically all children are born before their mothers are 40, and before their fathers are 50, the race has been perpetuated before we know that the parentage possessed the cancer factor."

Our own explanation of cancer inheritance is a hopeful one. For we know that there are certain familial lines in human heredity where

glandular exhaustion comes earlier on an insufficient diet than in others. It is possible by *proper diet* to prevent the development of goiter and of thyroid cancer, even in these susceptible lines. (See page 31.) As will be brought out elsewhere, the chemistry of cancers other than thyroid cancer involves the very same elements and growth acids which combine and cause wild growths in regions where irritation and faulty blood supply permit lumps to form.

Without possessing analyses that show chemical differences in their body fluids, we know that more than 90% of the breeding females of some strains of mice will develop breast cancer; while in other lines belonging to *low cancer* families, the incidence of breast cancer may be 5% or even as low as 3%.

Since 1936, J. J. Bittner has reported remarkable results from interchanging suckling mice. Newborn mice from cancerous mothers were transferred to foster-mothers of immune strains and remained healthy. Moreover, *their offspring* also proved cancer-resistant.

On the other hand, using females of a highly cancerous strain as wetnurses, Bittner learned that *nurslings from immune strains became cancerous*. The milk from cancerous mice was fed to weaned young of immune strains and produced cancer of the breast in them also. In his 1941 report (*Science*, May 30, 1941) Bittner describes tests in which he fed a preparation that had been made from frozen and dried cancer tissue. Since 6 of the 10 mice that consumed this filtrate also developed breast cancers, and the method used was similar to that known to preserve viruses, Bittner suggests that the "active influence" transferred usually by nursing may be a virus. (See page 39.)

The significant thing to us in connection with heredity is that Dr. L. C. Strong has been able to take mice with long continued history of ancestral resistance to cancer and to increase their susceptibility. He did not do this chemically, but by prolonging their lives. Thus strains of mice that ordinarily did not have an incidence of more than 5% cancerous individuals were so well nurtured that they lived beyond their normal life span. Then their susceptibility to cancer was raised to 35%. We have said that Strong did not increase susceptibility by chemicals. Yet, as we have shown, old age is accompanied by a weakening of the glands that control body chemistry. Of these glands we shall have more to say (page 155).

Dr. Macklin has concluded from statistical evidence in human cases that it is impossible to breed cancer out of the human stock. She says, "We apparently inherit factors for developing tumors at different times in our lives." Cancer immunity is the "late ringing of the cancer alarm clock." A man may die of some other disease at 55, and thus cannot be statistically included in the list of those who develop cancer at 70. He might have lived to 91 before he developed it, as the twins mentioned above. (Mumford, 1936.)

Dr. C. C. Little, Director of the Jackson Memorial Laboratory, and Secretary of the American Society for the Control of Cancer, has for many years been a student of inheritance in mouse-cancer. He has concluded from experiments that the evidence for heredity gathered from animal studies presents a much more gloomy picture than normal. The close inbreeding of mice is responsible for intensification and stabilization of cancer-preventing and cancer-inducing factors.

Little, in 1935, brought out the fact that cancer becomes frequent in the period when glands are old and their control of the body is weakened. His emphasis on the glands of internal secretion in combination with heredity is in accordance with the beliefs published by this writer since 1934. Little has *not* stated that failure of the glands to function is the key to cancer. Goiter has been known to affect 4 of a family of 6 girls. Examination of the records of thyroid derangement in some historical cases of breast cancer might disclose inherited thyroid weakness.

In 1928, Leo Loeb, whose work on ovariectomy and reduced cancer incidence we have elsewhere discussed, expressed his belief that "heredity acts merely as a limiting factor in the development of mammary cancer." He distinguished three types of relationships according to the relative preponderance of heredity and environmental factors. (1) In mammary cancer of mice, the stimulating agents acted on tissue which is apparently hereditarily sensitized so that it reacts to stimuli that themselves would be inert; (2) in certain mixed tumors of embryonal origin, heredity seems to be involved; (3) other tumors develop apparently only as a result of external stimuli. Thus Röntgen rays *seem* able to induce development of cancer of the skin, irrespective of previous hereditary predisposition. (But experiments showing such strain differences in response are lacking.)

One of the well-stated beliefs on cancer origin is that of Shaw-Mackenzie. He says, "Cancer belongs to a group of diseases in which there is defective fat-metabolism, and cholesteremia in particular."

The metabolism of fats and sterols is controlled by active glands of internal secretion. It is not unreasonable to conclude that there is an inherited weakness or strength in the glandular mechanisms which regulate tissue lipolysis. Ability to prevent accumulations of fats and fat-like sterols is determined by the glands of internal secretion, and here diet plays its part. Resistance to goiter can be easily induced, even in "goiter-families."

The various causes of cancer may all neatly fit into the picture, for cell chemistry in a given region is determined by glandular function, and it is subject to readily determined chemical and physical alterations which favor wild cell-growth. (See page 163.)

The Committee appointed by Surgeon General Parran of the U. S. Public Health Service to consider the cancer problem reported in the *Public Health Reports* for December 2, 1938, on heredity as follows:

"The tendency to develop cancer in a given family is confined for the most part to an organ or special tissue, so that we have lung-cancer families, mammary-cancer families, sarcoma families, and the like.

"An inherited tendency for endocrine disturbance may be the determining factor for one type of cancer; liver dysfunction may be prominent in another. Families not inheriting a natural tendency do not develop cancer from overstimulation with estrogenic hormones, or breast blockage."

Bainbridge (*Military Surgeon*, March, 1939) deplors the tendency to draw conclusions regarding human inheritance of cancer. He emphasizes the influence of lowered nutrition as a predisposing factor in cancer.

He says, "Rash and unjustified expressions on heredity in cancer tend to bring discredit on our profession, and are alarming to the general public. By the fear and mental anguish which they engender, we are well on the road toward developing a new disease—cancer-phobia, which can undermine the mind and bodies of the strongest of us."

CHAPTER III

Occupational Cancer

SUNLIGHT

Industrial hazards include exposure to the sunlight, which sometimes induces skin-cancer and frequently activates a quiescent mole. (Cf. Roffo, page 92.)

Light is credited with the development of cancer in farmers by Hazen who describes a typically dry "farmer's skin" as preliminary. But dust, products of decay, and even soot, may be contributory. Attempts to implicate the *tar* from adjacent roads have not been generally accepted as a cause of such cancers among agriculturalists.

Unna has described "sailor's skin" as especially prone to develop cancer. The sailor may develop cancer from sun exposure. Fishermen are likely to develop cancer of the lip from contact with tarred nets and lines. A noted Boston surgeon and cancer expert credited an old lady "quack" who had for some years treated sailors' cancers with an escharotic ointment and cured them. He also described the results noted by him after other well known men had used radiant energy, with *less success*.

A rare type of cancer nowadays is that reported a few years ago by Barth, called "cobbler's thumb cancer." It developed after repeated irritation by the cobbler's awl, sticking into the thumb, which was continually oiled with pitch.

The action of coal tar in causing experimental cancer in rodents has developed a large amount of research in the field of industrial hazards. And mouse cancer studies with agents that seem to accelerate or to retard the growth of tar cancers have been extensively publicized.

An abnormal liability to cancer of the lungs appears in workers exposed to coal, gas, tar, and tobacco. Experimental work with mice, in Campbell's studies of 1936, showed that 30% of the mice exposed to cigarette smoke developed cancer of the lungs. There

has been a great increase in *cancer of the lungs in women* since they took up *smoking* so commonly.

Miners who come in contact with radioactive dust, as in *cannel*, or *pit coal*, *briquettes*, and in *cobalt* or *pitchblende* mines, are frequently victims of lung cancer.

Matz, of the U. S. Veterans' Administration, citing records of 138 postmortems on cancer victims stated that nearly 40% of these cases of lung cancer had previously been engaged in occupations such as mining or metal working where the lungs were irritated. About 60% had suffered from influenza or pneumonia before the onset of cancer.

A common type of cancer among chimney sweeps is now little known. Dr. W. W. Keen cited a case in which a man who had been a chimney sweep 35 years previously developed at the age of 50 a typical soot-cancer of the scrotum. He died within a year. We may conclude from the evidence of clinicians that the resistance to a "new growth," kept up for many years, broke down when the glandular mechanism was no longer able to control, chemically, the local factors. Syphilis likewise paves the way for cancer by prematurely "aging" the tissues. (See page 27.)

Another type of soot cancer has been described, in which a gardener developed ulcers of the wrist at the point where his soot-laden pot handle had rested. The ulcers became malignant.

Leitch, mixing soot in an incubator with sebaceous fat, used a filtrate to induce epitheliomata in mice and rabbits.

Coal tars, and distillation products of coal including creosote, arsenic, anthracene, and aniline dye, will induce cancer. Aniline dyes cause cancer of the bladder; arsenic workers develop skin cancer.

Raw petroleum and raw paraffin induce cancer. The Belgian prisoners forced by Germans to work in their paraffin factories developed cancer of the hands (1914-1918 War).

Highly refined shale oils used to lubricate "spinning jennies" in the British cotton mills splashed over the middle of the bodies of the operators and for some years were known to cause cancer. During the past few years, these oils have been "hydrogenated," or otherwise *saturated*, and are not cancer-inducing. Such treatment will prevent the oils of an *unsaturated* nature from offsetting the elements which

in the blood tend to control growth, and prevent abnormal accumulations of cells and tissues.

Lyth in 1933 showed that the shale oils with the highest iodine numbers, that is, the ones that would naturally demand the most iodine and were the most "unsaturated," were the ones that induced cancer most readily in his tests with mice. (See page 207.)

Heat is a common irritant associated with the development of cancer. Locomotive engineers who are exposed to heat on the thighs are prone to develop cancer of the extremities.

A rather uncommon type of cancer has been reported in a baker. Here, heat and friction for 25 years were given as the cause of thumb cancer.

The classic example of cancer due to heat is that of the Kangri cancer in the miners of Kashmir who frequently hold a small coal stove to their abdomen and develop cancer in that region. This may be due to a combination of soot and intermittent irritation, it is believed.

In a small booklet by Dr. J. Clemmesen, the Danish Anti-cancer League has classified the cancer mortality from 1935 to 1939 according to age groups and occupations (Copenhagen, 1941).

Of the yearly deaths which were 140 per 100,000 population, records indicated high mortality in the *industrial groups*, in the age group 45 to 64. The agricultural groups showed low mortality from cancer.

TRAUMA

Mechanical injury is an extremely important industrial hazard, where chronic irritation of some region may be interspersed between occasional bruising blows. In his report to the Paris International Conference on Cancer, Barard cited traumatism (blows) in combination with an apparent predisposition toward cancer. In 328 carcinomas reported by him, 35 (10.5%) followed a single traumatism; 92 (28%) followed chronic irritation. Of 171 sarcomas, 35 (19.5%) occurred after a single trauma and 32 (18.5%) after chronic irritation. The late James Ewing, one of the sanest of our cancer authorities, recognized the fact that traumatic cancers due to a single injury are clinically attested; but he said, "traumas reveal more malignant tumors than they cause."

An important study of the medicolegal aspects of trauma and the development of malignancy was published in 1939 by R. J. Behan. (Relation of Trauma to New Growths. Williams and Wilkins Co., 1939.) Industrial compensation may be awarded for injury to the breasts of women who have gone into war-work so nobly in this emergency. But few of these women wear heavy protective shields.

Of a series of 100 cases of breast cancer, 42.33% were reported as due to blows. Injury to the ducts and blood vessels in the breast would pave the way for cysts and cancer. Adair and Bagg ligated the ducts at the nipple in mice, or prevented the young from suckling, and thus caused stagnation of the secretions and mammary cancer (Bagg, 1926, *Amer. Nat.*, 60, 234-239).

Breast injuries are more common (3 to 1) in men than in women, but the gland structure of a woman's breasts is such that they are more protuberant and more sensitive to traumatic injury. Carcinoma of the breast is in the proportion of 116 in women to only 1 in men (Williams).

Physicians reporting on accident cases believe that many cases of local injury occur which are followed some time later by malignant cancer, but that the original hospital staff and the attending physician rarely hear of the tumor that developed later.

Adams reported a case of a girl who developed synovitis of the left knee joint following an automobile accident. In three months she developed a swelling in the left knee-joint which arose from the bone, as shown by X-ray pictures. The diagnosis of osteosarcoma was followed by an order for operation. But the patient had developed metastases into the lung, and died.

Dr. W. B. Coley reported a case of a girl of 18 who was injured by the compression of her hand between two Pullman chair-backs, in a wreck. Eight weeks after the injury the hand showed a sarcoma and was amputated at the forearm. Six weeks later metastases in both breasts had been discovered, and the patient died two months later. Other cases of similar nature have been described and discussed in the paper by Dr. William Seaman Bainbridge, given before the Society of Medical Jurisprudence, in 1933, at New York City.

In the July, 1940, issue of the *Missouri State Medical Association Journal*, Drs. Leighton and Schmidtke have reviewed the history of

cancer cases at a St. Louis hospital with regard to the incidence of a single trauma as the etiologic cause. Seventy-nine case histories of definitely proved carcinoma with antecedent *single injury* were found. There were no instances where medicolegal or compensation questions were involved.

The single injuries reported by the patients were blows from wood, hammers, falls, razor cuts, burns from hot metal, cigarettes, or acids, laceration, and crushing injuries. Only 5 of the patients gave a history of familial carcinoma. Thirty-one of the cancers appeared in from 1 to 10 months after injury, and 42 others in less than 3 years.

With the shocking increase in cancer reported in the past few years, it is evident that greater attention must be paid to causes. Women in particular must avoid breast injuries.

At a recent conference, Dr. W. S. Bainbridge, discussing this book in manuscript form, told the author of cases in which some surgeons had been so brutal in their examinations that severe pain resulted from pre-operative manipulations of the breasts. He feels that there may actually be instances of metastases that have arisen by such rough treatment of tumors. One wonders if a benign tumor may not be rendered malignant by such tactics.

"I search after truth by which man never yet was harmed.
But he is harmed who abideth still in his deception and ignorance."

—MARCUS AURELIUS

CHAPTER IV

Parasites, Viruses, Temperature

PARASITES

Besides the mechanical irritation caused by their presence, certain parasites may, by chemical action, cause the development of tumors. There is a tendency to dismiss with little consideration the evidence for cancer production by certain parasitic worms. Yet the development of tumors in rats infested by certain roundworms was at one time given great prominence as an example of experimental cancer.

In 1913, Fibiger, a Dane, accidentally discovered tumors in the stomach in experimental rats. In these tumors he identified adult roundworms (Nematodes). Careful study of the possible source of the nematodes led to the discovery that they came from an intermediate host, the cockroach. He fed cockroaches to other rats, and was able to induce experimental tumors in their digestive tracts. The tumors formed in irritated regions in the stomach where the parasites (Spiroptera) were embedded in its walls. These gave rise to secondary growths in some cases, and the metastases did not contain the parasites. Truly this was a striking demonstration of parasitic production of a cancer capable of dispersal. And it deserves greater consideration, we believe, for parasitic worms are all too common, due to the food habits of some persons, and the laxity of food inspection in certain countries.

By feeding rats with the eggs of a tapeworm (*Cysticercus fasciolaris*), British investigators (1920) learned that cysts in the liver in some cases developed into sarcomatous growths. The Crocker Institute in New York has shown that some strains of rats are able to resist the carcinogenic actions of such infestations. This may be correlated with the diet, since faulty diets pave the way for lesions in the digestive tract. (See pages 77, 88.)

In Egypt and other parts of the Orient, a disease caused by the fluke *Bilharzia*, a flatworm, develops in persons who are parasitized after bathing in infested waters. The flatworm excretes eggs which develop in the body of a snail, and its larvae are able to burrow into the human skin and finally become carried by the blood to the liver. Ultimately they reach the rectum and the urinary bladder. In the urinary bladder irritation by the eggs gives rise to cancer in some cases. The troops stationed in Egypt in the World War were in a few instances victims of papillomata of the urinary bladder due to *Bilharzia*.

Parasitic worms may indirectly pave the way for cancer by causing defensive overactivity of the glands of internal secretion. In hookworm infestations *rickets* may occur caused by glandular hyperactivity.

VIRUSES

In 1912, Peyton Rous and J. B. Murphy of the Rockefeller Institute reported that an extract from a chicken sarcoma was capable of inducing a similar growth in another chicken. Previous students of transmissible cancers had used the cells and injected a macerate of them. But after removing the sarcomatous tissue, Rous and Murphy ground it up, and extracted it with a solution, finally filtering it free of cells. This extract, water clear and with no individual particles to be seen by the ordinary microscope, was so active that one drop of it caused the rapid formation of a sarcoma when it was injected into the breast muscles of another bird. This cell-free material caused the normal cells with which it came into contact to assume the character of sarcoma cells of the original tumor. Originally, this substance was believed to be a filterable virus. Rous and Murphy limited their terminology, however, to the word "agent," and later reported further studies that showed it was not a germ, or virus, but a *chemical agent*.

The Rous sarcoma is capable of being transmitted by the implantation of some of its cells, also, and it then behaves like other tumor transplants, and does not infect other surrounding tissues, as a filtrate might. There is no evidence that the Rous sarcoma has ever been

transmitted by direct infection of any other birds confined with diseased fowls.

Rous has worked with mammalian tissues, and extracted from certain papillomatous growths in rabbits a similar "virus." If injected into the veins of rabbits in which the skin has been irritated with tar, the "virus" is able to transform the growing cells of the injured region into cancerous cells. Rous has suggested that the virus may be a necessary condition for the development of cancerous growths in mammals as well as birds. Tissue cultures will continue to propagate these agents or viruses.

It is perhaps significant that such a virus may exert strictly chemical action. It is also worthy of recording again the fact that Mellanby has inactivated the Rous chick virus by *iodine* added to it. (See page 40.)

Dr. W. E. Gye, of London, working with the Rous sarcoma filtrate, tested it in highly diluted form, and finally concluded that continued ability to induce cancer was due to some *germ*, invisible with the ordinary microscope. He worked with an expert microscopist, Dr. Barnard, and this investigator found some extremely small particles in the clear fluid. He photographed them with the ultraviolet microscope, but they were too small to be stainable. Gye and Barnard concluded that the Rous chick sarcoma is transmitted by a filterable virus. But others do not subscribe to this belief and still adhere to the idea that the agent is chemical.

In *Science*, June 11, 1943, Thomas Francis, Jr. has given us a description of the chapter (lecture) on viruses and tumors in the "Messenger Lectures" book on Viruses and Disease.

Dr. Peyton Rous has shown that viruses each induce a specific type of tumor, whereas the type of tumor evoked by the carcinogens is primarily dependent upon the natural tendencies of the host and the nature of the receiving tissue.

Independently, Lumsden, Nyka, and Woglom have shown that in tumor-resistant animals which have been inoculated with cancer cells there are agents which retard new inoculations. Lumsden terms these *antibodies* or cytotoxins. That the effectiveness of the body in resisting infections is increased by glandular function, and that the *thyroid* and *adrenal* glands are related to the development of immu-

nity, has long been known. It is a fact that the antitoxin prepared from serum of horses with thyroid derangement has low antidiphtheritic value. Ablation of the thyroid glands in animals will lessen their capacity to form antibodies against typhoid bacilli (Farrant).

Alfred Taylor has for a time (1942) been using the yolk sacs of chick embryos in studies on the growth of transplanted breast cancers from DBA mice. Not only did ground cancer cells cause the tumors to grow, but Taylor and associates were able to secure from the tumors in the chick embryos a virus-like substance which, although free from bacteria and cancer cells, caused cancer to develop in healthy mice and in normal hen's eggs. (Taylor, A., *Science*, 97, Jan. 29, 1943.)

This discovery seems to be in support of the *virus* theory of cancer origin and transmittal. It does not exclude the chemical stimulation of cells to abnormal growth, however.

Heilman of the Mayo Clinic has tested Taylor's technique with 5 malignant transplanted tumors. One of these, a mammary carcinoma from mice, was implanted into the vascular area just beneath chick embryos and grew successfully. Emulsions from the yolk-substance of embryos that had thus become cancer-hosts were implanted into mice and then grew. Heilman comments on the difficulty from contamination with bacteria, which causes death of the chick embryos and lysis of the tumors. (F. R. Heilman, "Cultivation of the malignant cells in yolksac of embryonated egg." *Staff Proceedings of the Mayo Clinic*, vol. 18, no. 14, p. 223.)

It is of especial interest to note that Brown and Pearce, in 1923, found that the rats which proved most resistant to new tumor implants, after they had recovered from the first inoculations, were those with extremely active thyroid, adrenal, and reproductive glands.

Viruses furnish a factor that disturbs the chemical balance, it seems, for as stated (page 39) iodine inactivates them. The fact that injections of the fluid from cancers will cause other cancers to regress, indicates that *protective chemicals* are present in cancers, but in insufficient amount to slow down their growth. We have a similar condition when transient swellings occur, after attempts of the blood and lymph to control the region of a wound or infection.

FEVER-PRODUCING DISEASES

"Truth above everything." Evans Memorial, Boston.

As far back in medical history as the days of Hippocrates it was known that certain diseases which induce fevers were able to cure cancer.

Modern interest in this fact was stirred by the celebrated case of W. Busch reported in 1866. A woman with a far advanced case of multiple fast-growing sarcoma of the skin of the head, and with involvements of the lymph nodes of the neck, was under treatment at a Bonn Clinic. She caught an infection of erysipelas, developed a high fever, was extremely ill, and eventually recovered from the erysipelas. In the meantime, she was cured locally, and generally, of the sarcomatous cancers.

A few early students of the problem believed that bacterial toxins caused the cancers to regress. Coley's fluid, consisting of mixed bacterins, including the *erysipelas* organism, was developed by him in 1909. It was used for about 20 years, and several clinicians approved of it as valuable. It keeps the patients in a continuous state of fever; cancers may regress. (See also Biotin-avidin, page 106.)

Coley, in 1891, named scarlet fever, typhoid fever, and cholera as diseases that caused cancers to regress. Nicholas Senn (1895) had several cases in which erysipelas caused cancers to regress. Volkmann and Bruns in Germany had similar results in their practice (1895).

Bayon experimentally caused regression of mouse tumors by injections with the organisms carrying relapsing fever. In 1918, Rohdenberg reported 302 cases of sporadic recession of malignant cancers in patients who had erysipelas, smallpox, pneumonia, acute tuberculosis, and malaria. Of those cures following bacterial invasions, most came after erysipelas. Rabies has also been noted to cause tumors to cease growing.

Professor Cardamatis, of the University of Athens, found that in areas in Greece, where malaria appeared in his study from 1903 to 1933, the number of persons who suffered from cancer was markedly less than in those provinces that were free from malaria.

Experimentally, a number of cancer investigators have shown that in mice, filtrates from broth that contained various bacteria were able to cause the regression of cancer implants. Fogg, of the U. S. Public Health Service, in his report of January 17, 1936, also described experiments in which bacilli destroyed tissue culture preparations of mouse sarcoma.

Shear and associates (U. S. P. H. S.) have recently done some remarkable work with "the potent polysaccharide" from culture filtrates of the *Bacillus prodigiosus* of Coley, now termed *Serratia marcescens*. In a masterly presentation of the action of bacterial preparations on tumors, Shear and Perrault (*J. Nat. Cancer Institute*, vol. 4, No. 5, p. 461, April, 1944) have shown how hemorrhage and necrosis of transplanted and also of *spontaneous* tumors occurred.

The experiments described by Shear and Perrault indicate powerful action of the polysaccharide fraction on tumors induced in 750 mice by injection of 3,4-benzpyrene. The *rapid* necrosis of such tumors is followed by speedy death. Injections of the polysaccharide did not affect the whole tumor, parts of which are more resistant than others. We may consider the results most significant, and learn that clinical trials and important cytological studies will be reported later.

Our interest in the investigation is two-fold, for first the Lee Foundation is now working on various sugars from fruits, and second, we consider that such bacterial fractions and filtrates involve endocrine action, and chemical attacks on cancer.

In his book, "Cancer," published in 1931, Willy Meyer, always greatly impressed by Busch's case, and similar ones in his own practice, has attempted to show that the alkalosis in the untreated system of cancer patients is turned into *acidosis* by fever, arising from infections, or in cases where Coley's fluid was used. But Meyer goes further, for he attributes the beneficial acidosis to starvation, the administration of parathyroid extract, of calcium, and of acids. He naturally includes also the fevers that are induced by fever machines, called *hyperpyrexia* inducers.

Meyer believes that *acidosis* will dehydrate cancer cells, and will insure them the greatest amount of valuable *calcium*; on the other hand, he has shown that abnormal functioning of the sympathetic nervous system permits the influence of *potassium* to predominate

over calcium, and that then the serum *alkalosis* is greatest, and most favorable to cancer growth. Alkalosis according to Meyer favors the development of cancer and its spread; while acidosis prevents and cures cancer.

Several clinicians have pointed out the fact that a wave of commercial propaganda towards "alkalizing" is causing many people to dose themselves so that injury results. As a matter of fact the *blood* should be kept normally with a slightly alkaline condition, but the stomach requires hydrochloric acid for protein digestion.

On the one hand, we have the belief of Coley that erysipelas cures cancer because it brings about the activity of *antibodies* which are specifically opposed to the infective organism that causes cancer. On the other hand, Meyer's thesis is that the necessary condition of *acidosis* is produced by bacterial infection, and that cancer cannot grow in an acid medium; while *alkalinity* favors the appearance of a tumor "wherever a chronic local irritation is present."

Dr. H. C. Connell, of Canada, after preliminary experiments with enzymes which broke down cataractous lens proteins in the rabbit, finally developed a solution which, when injected intramuscularly, would break down human breast carcinoma. He called the solution, derived from certain bacilli, "Ensol." He has been glad to instruct physicians in his technique, and for more than 14 years has been able to help cases that the *Canadian Medical Association Journal* classed as "desperate, regarded as beyond the help of surgery or radiation." Ensol had been used intramuscularly and intravenously without ill effects until 1938, when 11 deaths were reported at Orlando, Florida, from "Rex, series 152," contaminated with tetanus germs.

The *Canadian Med. Assoc. Journal*, January, 1941, gives credit to Dr. Connell for valuable findings with his Ensol, and quotes the Ontario Commission reports on its apparent value. *Tetanus* contamination occurred but once.

It should be noted that the use of Coley's fluid, of Witte's peptone, of foreign proteins, likewise secured strong adherents. Enthusiastic reception of any remedy for cancer must not be expected. For many deaths come because the disease was not identified early, or was not treated properly.

The *Journal of the Am. Med. Assoc.* (June 21, 1941) deplors the use of doubtful products to the exclusion of generally accepted procedures. For standard technique might control some early stages.

It must be stated here that any *serum* which is injected into patients that are far advanced in cancer may cause *anaphylactic shock*. All such patients are extremely susceptible, because their whole glandular mechanism has taken a terrific beating for the duration of the disease.

Early in 1940, the writer, while in Canada for a time as expert on mineral balance to the Maritime Fisheries, was fortunate in being invited to address the Ontario Commission on Cancer, in Toronto. Certain members of the Commission had read his published papers, and the way was open to present evidence on causes and different treatments to an earnest and well-informed group. It was pleasant to be *invited* to talk to the august body before whom many have been ordered.

After the discussion, at which the writer urged the careful investigation of any promising remedy, one of the members of the Commission stated that the serum treatment of Dr. J. E. Hett, of Toronto, was under consideration by that body, and that he personally had seen cases and case reports that were in support of claims made regarding its value.

The head of one of the Toronto military groups, the Legion of Frontiersmen, a personal friend of the writer, had previously mentioned a case in his own office family where Dr. Hett had definitely saved a life in curing cancer. Accordingly, when an invitation came from Dr. Hett and his friend, Dr. G. R. Philp, to discuss with them cancer treatment, it was accepted at once.

Dr. Hett's serum is diluted with about $\frac{1}{2}$ cubic centimeter of distilled water and injected intravenously once or twice a week for an average of about thirty injections. Case records indicate recoveries and a worthwhile attack.

The serum injections cause first, in about an hour, a *chill*; then a *fever*, the whole reaction lasting not more than 6 hours. The severity of the malignant growth determines the degree of the reaction. During his use of the serum for more than 12 years, Dr. Hett has records of patients alive and apparently normal for 11, 10, 9 and 8 years

after treatment. Dr. Hett believes in surgery—the cancerous mass should be cut out. He prefers cases which have had no X-ray treatment.

There are, according to Dr. Hett, at least three factors involved in the development of cancer. First, chronic irritation; second, an imbalance of the endocrine organs; third, the presence of an ultra-microscopic germ or virus. Some of his work on the blood supports his virus theory.

Dr. Hett, in his book "Cancer" published in 1943, says, p. 186, "An individual does not develop cancer if his endocrine glands are functioning normally, even though there be an irritation present which otherwise might be fit soil for cancer."

The writer was impressed strongly by the open-minded attitude of the Cancer Commission, who seem anxious to survey the possible beneficial treatments and therefore invited a stranger to tell them what he had learned; second, because Dr. Philp, a former member of the staff in Pathology at the University of Toronto, had jeopardized his own reputation in entering on an evaluation of the work of a doctor with a "new" cancer remedy; third, because through hard work in marshalling evidence of successful treatment, Dr. Philp had made it possible for Dr. Hett to be reinstated as a physician, after he had been expelled from practice. The restoration of his rights, through an Act of Parliament, the keen interest in his serum that is exhibited by the Cancer Commission, and by clinicians in the United States as well, constitute a triumph for fair play.

It is with a great deal of satisfaction that we note from a letter written by Dr. Hett in May, 1940, that he is now using calcium and iodine as adjuncts to his treatment, as we suggested.

A great drug company is now investigating the Hett treatment, after studying the data presented by him. Full details of his method have been furnished to the Provincial Cancer Commission, Ontario, Canada, by Hett.

Dr. D. T. Quigley, while he is not dogmatic about the causative organisms that are responsible for cancer, has emphasized the fact that infections which provide cancer soil must come through the blood stream.

He says, "The steps in the development of cancer are plain. First, injury of a chemical, thermal or mechanical nature, which breaks down Nature's protective wall of epithelium. Second, a repetition of the same insult before the protective walls have a chance to heal. Third, invasion of the injured area by microorganisms which establish themselves and continue to grow. Fourth, the continuation of the chemical, thermal or mechanical insults. Fifth, the building up of a great wall of cells as a defense measure to shut out the invading organisms and the loss of inhibition in this mass of cells which permits them to grow indefinitely. This wild anarchistic cell growth is the disease we call cancer."

He says in his book "National Malnutrition," "The part of a body on which a cancer grows has a special soil on which the invader finds a favorable environment." "Whether the immediate cause of cancer may ultimately be found to be a virus, a fungus, a bacillus, or a chemical compound makes little difference in the question of prevention, since the clinical facts show that previous local disease must exist before a cancer growth may be started. The important fact is that the diseased area on which the cancer finds its suitable soil must not be allowed to exist. Efforts to cut down the incidence of cancer will be completely successful if we can eliminate these precancerous areas of local disease."

Unfortunately, Gye and associates have resisted attempts of W. Mitchell Stevens and others in Britain to interest them in the rôle of adequate dietary and mineral treatment of their animals. As already pointed out, Mellanby has inactivated the Rous chick sarcoma with iodine. Viruses, like bacteria, may be destroyed by the products of adequately functioning glands of internal secretion, and "spontaneously" the tumors may regress.

The clinician Dr. W. Held of Chicago has said, "Cancer is most uncommon in those who have been afflicted with germ disease in their pre-cancer years. It appears that, given a perfectly functioning glandular system, invasion, particularly repeated invasion of the system by germ disease or toxic conditions, steels the system and invokes defensive properties which are active in the prevention and cure of cancer."

We may suggest appropriately that the *survivors* of such infections have a *strong defensive* mechanism. Serum of low antitoxic value in diphtheria and low iodine content is obtained from horses that have developed thyroid malfunction. Held believes that the anti-cancer effect of fever-producing diseases is due to the release of defensive properties and the "re-establishment of erstwhile arrested functions" in glands. This recalls the report by Pringle that vaccines and protein shock affect the thyroid-adrenal apparatus and the "sympathetic fever" thus produced is the normal reaction against infections. In tuberculosis the thyroid gland is especially active, and cancer does not develop, this writer believes, because of the cholesterol-inhibiting effect of iodine.

High temperature itself is involved in the "spontaneous" cure of cancer after infections. And high temperature or "sympathetic fever" is the normal reaction of the body against infections. In his book, "Fever, Heat Regulation, Climate, and the Thyroid-Adrenal Apparatus," 1928, W. Cramer has brought out the fact that the increased heat production in cases of infections involves stimulation of both the *thyroid* and the *adrenal* glands.

In comparing the cancer deaths in South Carolina with states where cancer mortality is three times as great, some cancer students with no knowledge of thyroid cancer have attributed the differences to *climate*. But South Carolina is called the "Iodine State."

Fuller, Brown, and Mills, in *J. of Cancer Research*, June, 1941, reported the influence of temperature on mice of cancerous strains. In a control room with temperature from 70 to 94 degrees 66 mice were placed. A hot room received 67 mice kept at a temperature of 90 degrees. A cold room with temperature kept at 65 degrees received 67 more mice. The mice were about 8 weeks old and received the same diets.

At the end of 20 months, 19 tumors had developed in the cold room mice, with about the same number in the control chamber. The *hot room mice* had only 5 cases of tumors, with 62 non-tumorous.

Cramer says, "The rationale of the so-called non-specific protein and vaccine therapy would be that it elicits an increased functional activity from the thyroid-adrenal apparatus; in fact, sympathetic

fever, which is one of the normal reactions of the body against bacterial infections."

The fact that iodine is the key element in many reactions that have been identified with the adrenals, the pituitary gland, the sex glands, as well as the thyroid, has been brought out by the author in a series of articles. (See Chidester, 1934, "The relation of iodine to the effectiveness of endocrine extracts." *Archives Internationales de Pharmacodynamie et de Thérapie*, volume 48, Fascicles III et IV, 1934.)

The selfsame glands which furnish extracts that increase the power of the blood to resist disease are those which show high iodine content. They all when normally active are able to mobilize calcium as well. Iodine release from glands permits direct action of the extremely potent combination, iodine-trichloride, on the fatty coverings of bacteria. Iodine action on diseased tissues is well known, and its selective union with and destruction of cancerous growths have been experimentally proved, and clinically demonstrated.

Glandular activity and the cellular release of iodine are followed by a mobilization of several other elements that are known to cause cancer regression. Fevers actually cause the chemical defense-mechanisms to attack tumors, and to break them down. On the other hand, it seems evident that a long series of diseases will age prematurely the glandular organs and ultimately permit the invasions of cholesterol and other growth-substances which characterize gallstones, cataracts, arteriosclerotic blood vessels, and the most malignant cancers.

The fact that "acidosis" has been linked with cancer recoveries, while alkalosis is found in certain untreated cancer cases, leads us to our consideration of acid producing and base producing diets. (See page 67.)

LOW TEMPERATURE

It has long been known that exposure to cold induces *overactivity* of the thyroid and adrenal glands. Stimulation by such means is beneficial if not too long continued; on the other hand, it may result in glandular exhaustion, after a time.

In 1919, Fabry reported that when *carcinoma* of the skin was frozen with carbon dioxide snow, and then treated with X-rays, with reduced doses, healing took place in 3 to 4 weeks.

Since 1938, Fay and Smith of Temple University have been treating cases of drug addiction, mental disturbance, and cancer, with reduced temperatures. They purposely selected the hopeless, terminal cases of cancer and were able to reduce pain. In the case of local application of low temperatures to human cancers, they found not only that pain was relieved, but also that some of the lesions were reduced in size. Local low temperatures were from 40° to 50° Fahrenheit; in 33 cases where chopped ice was used to pack the whole body, the temperatures ranged from 90° down to 74° Fahrenheit.

Appropriate precautions were taken to insure proper fluid and salt balance. The routine duration of a generalized low temperature treatment was from 4 to 5 days. The initial use of ice to lower the temperature is ordinarily followed in about 2 hours by blankets and ice bags. A small dose of the anesthetic "evipal" is given to prevent shivering and general sensations of cold in the early period.

Fay and Smith are not presenting "hibernation" as a cure, but merely as a palliative, and to relieve pain in advanced cancer. Like all clinicians who attempt to deal with cancer, they have been besieged and entreated, far beyond their limited facilities and strength, to help the hopeless, inoperable cases. Their technique has been tried by others with the same general results, relief of pain. Patients who had been receiving doses of sedatives as large as 5 or 6 grains of morphine a day, were able to eliminate sedatives after refrigeration. In some cases there was a measurable increase in the size of the cancers in from 24 to 48 hours. In August, 1939, Smith and Fay reported two cases of *mammary cancer* in women of about 30 in which complete disappearance of the local lesions occurred. One had then remained free from recurrence for 2 years; the other case had for 1½ years been free of her breast cancer, and metastatic skeletal lesions were repaired. Their "hibernation" technique is potentially valuable in many diseases that involve glandular function and the rate of metabolism.

"Few things are impossible to diligence and skill."

—JOHNSON

CHAPTER V

Nutrition

"All truth is safe and nothing else is safe; and he who keeps back the truth, or withholds it from men, from motives of expediency, is either a coward or a criminal, or both."

—MAX MÜLLER

Cancer is the only major disease involving lowered vitality, and even anemia, in which dietary and medical adjuncts to other methods of treatment have not been fully utilized. Surgery and radiation are the acceptable direct attacks, but they require supportive treatment to hasten recoveries.

The reason for this attitude, in which diet and medication have been given insufficient consideration, is because every able surgeon knows that early operation will prevent a cancer from spreading through the body as metastases. He realizes also that through fear of an operation some patients will temporize with faddistic diets, suggested by quacks, until their cancers may reach a hopelessly inoperable stage.

Radiologists, noting how completely certain cancers will disappear after treatment with X-rays or radium, have not appreciated the rôle of elements that are activated in the body to destroy malignancies. Nor do they realize the necessity for restoring a physiological balance that has been disturbed by the chemical requirements of a cancer, and also by irradiation. Neither surgeons nor radiologists have had the opportunity to evaluate drugs and diet, which the general practitioner naturally obtains through experience.

The U. S. Public Health Service, in bulletins on cancer, has attempted to inform the public, and to reduce quackery. Thus—
"Many absurd ideas regarding the relationship of diet to cancer are prevalent. Neither a high protein diet, a vegetarian diet, nor over-indulgence in any type of food has any demonstrable effect on cancer incidence. On the other hand, clinical evidence suggests that poor teeth, or lack of teeth, the ingestion of hot food and drink, irregularity

of meals, and gastro-intestinal diseases may be of some importance in the causation of stomach cancer."

There is considerable evidence, however, that proper diets will prevent the development of cancer; that growth of cancers is retarded by some diets; and that, in conjunction with the generally accepted treatments by surgery and radiant energy, even advanced cases of cancer are benefited by foods tending to normalize the body.

Cancer patients continually lose essential minerals, and when they are subjected to operations or to irradiation such losses are increased.

True it is that the experimentalists on mouse cancer differ markedly in their evaluation of minerals, vitamins, and foodstuffs in general. There are excellent reasons for such divergent reports. They are characteristic of many physiological tests, performed under varying conditions.

Barker, of England, has for years contended in books and articles that one of the chief causes of cancer is *vitamin-deficiency*. But Copeman, of the British Ministry of Health, has been just as firm in his belief that cancer is related to vitamin *excesses*. Both of these gentlemen are presumably correct. For excessive sunlight (Vitamin D) will induce cancer; and adequate Vitamin A will offset Vitamin D, in experimental animals, preventing various degenerative conditions *other than cancer*. Moreover, glandular normality is achieved by proper vitamin balance; while a lack of vitamins, or an excess of certain ones, will cause profound glandular derangements.

A general principle which we wish to emphasize is that the very same agent that may, in proper amounts, balance minerals and *aid* the glands in restoring animals and human cases to health is capable of being altered chemically, or of being used in such *amounts* that it will set up derangements of function, and pave the way for cancer. This has been brought out clearly in connection with vitamins, fats, and minerals, tested experimentally with reference to cancerous mice.

Let us consider the common type of cancer, affecting the thyroid gland. It is in a large percentage of cases preceded by adenomatous goiter. Thyroid cancer metastasizes to the lungs, breasts, ovaries, brains, bones, and even to the viscera. Authorities who would have us ignore diet as a factor in cancer are asking us to eliminate our

common sense. And—"Science is trained and organized common sense."

Goiter is known to arise from bacterial infection, and is early produced in vitamin-deficient animals. It has been experimentally induced by diets lacking iodine and rich in fats; or carbohydrates; or proteins. Excessive amounts of calcium, chlorides, or iodides cause goiter. Goiter is related to the mental state, and diet is here again contributory, for hyperthyroidism and disturbed mental states appear in animals that lack certain vitamins and fats.

Dr. W. Mitchell Stevens of Cardiff, Wales, has said, "Cancer is essentially a deficiency disease, comparable to goiter. The key to the cancer problem lies in the dietary, *really*, though not *apparently*."

OBESITY

Dublin, of the Metropolitan Life Insurance Company, has cited statistics showing the relationship of overweight to cancer. Men over 45 with moderate overweight showed a 9% greater mortality from cancer than those of average weight, for the same age. When the excess weight was from 15% to 24%, the cancer death rate was 24% higher; men of 25% and more, overweight, suffered a cancer mortality of 30%, as compared with those of average weight. Dublin says, "Cancer may be a reflex of internal maladjustments, of which overweight is one of the outward signs."

In Holland, mortality from cancer of the stomach is especially great. This has been attributed to the fact that Hollanders are heavy eaters, that they bolt their food, without sufficiently masticating it, and that they use large amounts of tobacco and spirituous liquors. Hurst has stated that chronic gastritis—chronic irritation—is responsible for about 65% of the cases of gastric carcinoma.

One of the most striking examples of change in dietary habits associated with a great increase in cancer is that in Denmark. Hindhede, of Copenhagen, was made Food Controller of Denmark during the World War. He placed his people on a diet that was low in proteins, but which contained whole-wheat bread, with its bran, combined with butter and potatoes. Alcohol, tea and coffee were almost

unobtainable. The death rate fell to the lowest level seen in any civilized country, viz., 10.4 per hundred thousand. When the great influenza epidemic swept the world, Denmark was the least affected, its death rate being lowest in Europe.

After the World War, the Danes returned to their earlier, rich fare. Highly spiced and salted foods were consumed in huge amounts, and obesity became again very common. In 1928, the death rate from cancer rose to 1 in every 5 persons above the age of 45. And the death rate from all diseases exceeded that before the War. Let it be understood that the wartime restricted diet may have paved the way for death from "old age" at 50.

Some years ago, Hoffman, statistician for the Prudential Insurance Company, learned from questionnaires that a large proportion of cancer patients admitted being heavy eaters, particularly as regards meat and sugar. And a large proportion, about 25%, also reported the occurrence of rheumatic affections. The glands of internal secretion are involved in the development of obesity; of rheumatism; and of cancer, after dietary excesses.

Koch has reported in 50% of his cancer cases a pregrowth obesity which may have started 10 years before the cancer appeared. He also secured a history of previous thyroid disturbance, overactivity of the gland giving way to hypothyroidism (lowered function) before the cancer growth showed itself.

INTESTINAL STASIS

The first clinician to emphasize the relationship of intestinal stasis to cancer, insanity, and various glandular diseases, was Sir Arbuthnot Lane. Like other pioneers, he was viciously attacked, and his reports on an extensive list of diseases caused by intestinal self-poisoning were discredited. But many able clinicians have proved the correctness of his claim, and it is definitely known that remedying intestinal stasis has cured many cases of malignant and non-malignant growths which did not yield to other treatment. Mammary cancer and thyroid cancer as well as rectal cancer are included in the reported cures by such means.

Lane* has emphasized the fact that refined and concentrated foods, from which the life-giving vitamins and the indispensable mineral salts have been eliminated, now form the staples of peoples' dietary, and "such foods inevitably lead to constipation." He says, further, "I am convinced that *cancer* almost invariably arises only in tissues where vitality has been sufficiently depreciated by chronic intestinal self-poisoning, or by syphilis. *Cancer never* attacks a *healthy organ*."

Our general thesis on the relationship of glandular condition to the availability of those elements that break down cancers is supported by the clinical reports of Lane, Rowell, and Macy. For these physicians have independently shown that without relieving intestinal stasis their attempts to cure thyroid derangements were not successful. The Belgian, Hertoghe, first brought out the relationship between intestinal stasis and thyroid insufficiency. Sir Robert McCarrison has shown how the accumulation of feces will cause overactivity of the thyroid and subsequent diarrhea; but that this is followed by reduced thyroid function, and even more persistent constipation.

Clark has been able to benefit human senile cataracts by correcting the intestinal function. Lens cataracts consist of cholesterol accumulations, and the *most malignant cancers* consist largely of cholesterol. Thyroid extract has proved beneficial in human cataracts (Kerr); and is well known to be valuable in the treatment of arteriosclerosis. Since cholesterol accumulations in arteriosclerosis, as in cancer, are signs of "old age" in the tissues involved, it is not surprising that diet and glandular therapy controlling cholesterol will prove curative in these diseases.

PROTEINS

Growing cancers contain derivatives from proteins, carbohydrates, and fats, and they also contain the fat-like lipoids. The proportion

* A few years ago, in New York City, Dr. William Seaman Bainbridge, in his introduction of Dr. Lane to the group of medical men who gave a dinner in his honor, said, "Dr. Lane, like others who have pioneered, you went through three stages: first, they said 'Your statements and evidence were ridiculous, and couldn't be so'; then they said, 'Well, there may be some truth in your theory,' and finally, 'Yes, you're right, but *we knew it all the time*.'" And Dr. Bainbridge in his successes always gave credit and honor to Sir Arbuthnot Lane.

of mineral constituents found in the body fluids varies considerably from time to time in cancers according to their age and speed of growth.

Proteins, derived from meats, but also from plant foods, yield about 25 "building stones," the amino-acids. Some of these have been shown to stimulate the growth of experimental cancers in animals. (See pages 55-59.)

About 25 years ago, Dr. L. D. Bulkley, of New York City, concluded that "meat is the precancerous diet." He had organized and built up the New York Skin and Cancer Hospital, and he wished to set aside a department of that hospital for the non-surgical and dietary treatment of cancer cases. Such violent opposition arose, and so thoroughly was he discredited, that this able physician was forced out of the hospital. He gave his patients extracts made from vegetables, by boiling down the water in which they were cooked. He was convinced of the value of *potassium* in cancer. (See page 123.)

Dr. Henry Smith Williams, in a book, has given the reports of some 1200 physicians, who cured more than 3000 cases of cancer without radiation or surgery. They attributed cancer to *excessive protein intake* and the resultant intestinal toxemia. We know that there are putrefactive protein derivatives in the lower bowel, in cases of intestinal stasis.

Eskimo Diet (Eskimo means "raw meat-eater")

The conclusion that meat, as such, may cause cancer is not supported by evidence collected by a number of physicians, and explorers, from studies of the food habits of the Eskimos of the old days.

Nicholas Senn, the great Chicago physician, showed some 50 years ago that the Eskimos, termed by him "the healthiest people in the world," lived on an exclusive meat diet, and yet were immune to malignant cancer formation. And Thomas, who has reported on the immunity of Eskimos of earlier days to vitamin deficiencies and cancer, stated in 1927 that they subsisted on lean meat in higher proportion than was generally believed. (See Stefansson's meat diet, Section on Fats, page 67.)

The fact that high protein diets furnish amino-acids that bind iodine has been suggested as a cause of experimentally produced arteriosclerosis. The writer has related this to thyroid disease, which precedes certain types of cancer and, as we have already shown, is linked with intestinal stasis.

The reason why *proteins* in the diet of the Eskimos do not induce thyroid overactivity and subsequent early exhaustion is that they are thoroughly *iodized*, we believe, and that large amounts of iodized fats are included also. Carter, in 1924, emphasized the protective action of iodine in the foods of Eskimos against thyroid disturbance. He also brought out the effect of a lower temperature in preventing *protein putrefaction*. In identifying iodine action to protect against thyroid disturbance and cancer in the meat-eating Eskimos, Carter antedated our own thesis. We have emphasized the great importance of the fat-thyroid-iodine balance, and the *fats* in diets of denizens of the far North.

A corroborative note on iodine in the diet of the "old" Eskimos before they took over white man's incomplete diets has been furnished by Price, the distinguished dental surgeon and student of the diet of primitive peoples. Dr. Price reports that in olden days the Eskimos ate foods that contained 97.8% more iodine than today. Their proteins, fats, carbohydrates, and lipoids were all adequately iodized; increased oxidation occurred, and abnormal accumulations would be impossible.

Experimental Evidence from Amino-Acids

In the present World crisis, with its increasing difficulty in securing adequate amounts of *animal proteins*, there is naturally great interest in determining which proteins are most necessary. This naturally brings us to a consideration of the amino-acids, which are the *only indispensable substances* that are *obtained from proteins*. The amount of specific amino-acids needed will naturally vary with the age of the individual, and with the source of the proteins. Proteins must also be considered in relation to the carbohydrates, fats and minerals in the diet, and must vary in accordance with the activities of the person under consideration.

In milk, the protein content is from 20% to 30% of the solids. Dr. Roger Williams ("Introduction to Biochemistry," 1931) states that when casein from *cows' milk* is present in an amount equivalent to 18% of the total food, all of the required amino-acids are present in sufficient amounts for satisfactory nutrition of rats. But when this proportion is cut in half (9% of the total food) normal growth fails to occur. The addition of a small amount of pure *cystine* induces normal growth.

Some proteins are inadequate, even when fed in large amounts. These include gelatin, zein, and gliadin. Gelatin, so highly advertised over the radio, lacks the amino-acids tryptophane, tyrosine (important for the thyroid and adrenal glands), and cystine.

Certain vegetable proteins may be unsatisfactory sources of the requisite amino-acids. These must be supplemented by animal proteins or by specially selected vegetables which do supply the lacking amino-acids.

Amino-acids furnish the "building stones" for the construction of tissue proteins, aid in the synthesis and activation of enzymes, and are growth acids.

Tyrosine and possibly phenyl-alanine are precursors of the internal secretions of the thyroid and the adrenal glands.

Thyroxin bears a close chemical relationship to tyrosine. Adrenalin resembles tyrosine more closely than any other amino-acid. Thus the two glands that are most disturbed in infections by profound changes in temperature, or by fright and anger, require an amino-acid for their hormones. And Vitamin C, which is vital to the normal function of the thyroid, is related also to tyrosine.

Choline is related to the amino-acid cystine. Dr. W. H. Held of Chicago says, "Choline or cholesterin poisoning as a cause of glandular sluggishness has been dwelled upon by me, in several articles." (Held, *Amer. Med.*, June, 1924, pp. 339-348.)

Doctor Held has for many years used iodine in the treatment of precancerous and cancerous conditions. He advertises his "Iodo-Held" to physicians.

Hammett and Voegtlin have independently shown that *glutathione* stimulates the division of normal cells, accelerating the growth of their cell-nuclei.

Glutathione is an organic *sulphur* compound, closely related to the proteins. It is composed of three amino-acids, cysteine, glycine, and glutamic acid. Hammett, discussing glutathione and developmental growth (*Science*, 79, May 18, 1934, p. 457), says, "The chief function of cystine or its reduced form cysteine is the acceleration of cell multiplication. This derives from the SH (Sulphydryl) group therein." Glycine promotes regeneration in certain marine animals, tested by Hammett. He considers it to be important in protein re-constitution favorable to regeneration and the rebuilding of muscular tissue. Glutamic acid "accelerates the selective building up of the protein molecule which is the characterizing process of differentiation and its consequent organization."

Glutathione, which has engaged the attention of cancer workers at the Lankenau Hospital, Philadelphia, and at the U. S. Public Health Service's Cancer Institute, is known to induce remarkable stimulation in the growth of *cancers* in mice. The glutathione was subcutaneously injected daily in Voegtlin's tests.

Cystein brings to glutathione the SH combination that characterizes the *sulphydryl* group. And this group is exquisitely sensitive to oxidative agents, as shown by Hopkins and Dixon (*J. Biol. Chem.*, 1922). Thyroid secretion determines the amount and distribution of the amino-acids, and it is known that after thyroidectomy glutathione in the blood is increased. With an *overactive thyroid*, blood-glutathione is decreased.

Several iodine compounds are known to inactivate glutathione in chemical tests. Lohmann (1933) found that iodo-acetate destroys glutathione.

Hammett has discussed the sulphydryl group (including glutathione) in the light of Dr. F. X. Dercum's observation (corroborated by the Mayos) that malignant disease is infrequent in persons while they are suffering from *hyperthyroidism*.

Hammett says (*Arch. of Pathol.*, 1929, vol. 8, 575-), "This negative correlation might be predicted from the known facts relative to thyroid function and sulphydryl lability. It is well known that metabolic rate is regulated by the level of thyroid activity, and that when this is increased the oxidative processes of the body are enhanced. It is a fact that sulphydryl is exquisitely sensitive to oxidiz-

ing agents. Hence the chance for development in a person with hyperthyroidism of a sulphhydryl concentration adequate to produce malignant cell proliferation is limited."

In experiments with various amino-acids, the group associated with Dr. C. Voegtlin, at the U. S. Public Health Service's Cancer Institute, compared the effects of tryptophane, lysine, cystine, zein, and glutathione on the growth of young normal mice and on tumorous animals.

Lysine accelerated cancer growth in mice; and when it was lacking in two of the experimental diets, spontaneous cancers of the breast were remarkably inhibited in growth.

Dr. C. Voegtlin ("Some chemical aspects of the cancer problem." *Science*, 1938, vol. 88, pp. 41-48) states that a *zein* diet, even when supplemented with small amounts of *lysine*, caused a marked *retardation* in growth of mouse cancers. When *tryptophane* was added, tumor growth was *accelerated*.

It is interesting to recall Williams' previous statements on the importance of added *cystine* in the growth of rats on restricted diet, where the supportive 18% of amino-acids had been reduced to 9%. (See page 57.) For Voegtlin reports that a diet containing 17% of dried whole milk powder proved inadequate for the *growth* of normal young mice, or for *tumor growth*. In each instance there was deficiency in amino-acids. But when 0.4 to 0.6% of *cystine* was added, the young mice grew normally, and tumor proliferation was markedly increased.

Cystine has been inactivated by *iodine* in tests made at the Lankenau Hospital, Philadelphia, by Shinohara.

We must not fail to record evidence of the usefulness of sulphhydryls in the treatment of wounds and ulcers. Brunsting and Simensen, of the Mayo Clinic, in discussing the effect of sulphhydryls on cell growth (*Jour. A. M. A.*, 1933, 101, 1937-) report that *cysteine* (the reduced form of cystine) proved extremely valuable in the treatment of ulcers and of slowly healing wounds.

Arginin accelerates cancer growth. Gilroy (*Biochem. J.*, 1930, vol. 24, 1181-) was able to inhibit tumor growth in 165 mice with thyroxin. But arginin balanced this effect, and permitted the tumors to grow.

To sum up, *proper amino-acid intake would seem to be necessary, while the assurance of adequate iodine to keep the thyroid gland normal is also indicated.*

Of the several undigested proteins commonly found in the feces, two have been used in experimental cancer. Stoecker and Wacker prepared solutions of indol and skatol in rabbit fat, and induced cancerous growths in rodents with them. (See page 55.)

Two of the most distinguished cancer experts in the world (one British and the other American) have furnished evidence that not only rectal cancer but breast cancer has been cured in hundreds of cases by relieving *intestinal stasis*. This may involve the products of protein putrefaction and, as we have already shown, is clearly related to glandular function, especially thyroid action.

Early manifestations of gastric disturbance appear in cancer patients. The fact that inadequate hydrochloric acid is present permits *undigested proteins* to accumulate in the large intestine. The vicious circle is established, for intestinal stasis arises when thyroid disease is present; but thyroid derangements arise as a result of accumulated feces. When there is an adequate intake of iodine, the important process of desaturation of fats by the liver is efficiently carried on. Then it is that the unsaturated fats go to storehouses, and the *bile* is rich in *iodine*. Statements made regarding the small amount of iodine needed in the human body do not recognize the considerable amount excreted in feces, urine, and through the lungs and skin.

For 15 years, a distinguished clinician has informed the writer he has used colloidal iodine in rectal cancer. His records also include breast cancers that have remained cured, without recurrence, for more than 12 years after iodine treatment. He has long known that iodine itself is radioactive, but has also used irradiations by X-ray and radium.

CARBOHYDRATES

Glycogen, a carbohydrate from the liver, found in large amounts in muscles, is converted into lactic acid. Lactic acid, which easily penetrates cells, may be an important factor in the destructive action of malignant cancers on surrounding tissues. Moreover, retention

of lactic acid interferes with muscle function, and thus with circulation of necessary elements and foods.

Okuneff learned that the lactic acid produced in tumors by glycolysis exerts a profound influence on the acid-base balance in the tumor, and affects the whole organism. The younger the tumor, the greater the lactic acid. The outer portion of the tumor was more acid than the central portion.

Borrel and deCoulon, in 1922, noted that the glycogen content of tumors parallels their malignancy and speed of growth. They knew that glycogen has a great affinity for iodine. Accordingly they used an iodine and glycogen combination in tests on animals. From 5 to 15 subcutaneous injections of *glycogen-iodide* caused dissolution of tumor transplants; injections of glycogen alone promoted greatly the growth of the tumors.

Cramer learned that insulin was absent from malignant growths, though present in appreciable amounts in normal tissues. Shirlaw and others have cited cases of cancer that appeared in patients who had a previous history of incipient diabetes. And insulin has been used in human and experimental cancer with benefit. Thyroid extract and the iodides have been used to increase the size and number of the "islets" of tissue in the pancreas which furnish insulin. The interrelationship between glandular function and the handling of essential foodstuffs is one of the keys to the chemistry of cancer, we believe.

Cancer cells were shown by Warburg to exhibit an excessively high rate of fermentation, and to cause a vastly greater amount of sugar to be split into lactic acid, than in the case of normal cells. Cancer cells have also been shown in experimental studies to require very little oxygen. Here again we have experimental evidence of the value of iodine, for thyroxin (65% iodine) has been used in experiments where chick cancers were killed by exposure to *oxygen*. The thyroxin greatly hastened the speed of the oxygen poisoning.

Cancer cells are capable of splitting *dextrose* to lactic acid, producing in one hour an amount of lactic acid equal to 10% of their weight. From 50 to 70% of the glucose from circulating blood is removed by tumor tissue, according to Warburg, in his studies with the rat. Experiments by Cori and others show that the blood leaving

a chick cancer contains from 2 to 3 times as much lactic acid as in the blood that entered it.

Deeks, noting that cancer patients generally give a history of an unbalanced diet and a series of disturbances emanating from the alimentary tract, states, "These are practically all due to an excessive consumption of carbohydrates, and a deficiency of green vegetables."

Beebe learned that after a course of feeding a diet free from carbohydrates his experimental rats were extremely resistant to the Buffalo-sarcoma. Sweet found that a carbohydrate-free diet increased resistance to cancer implants.

Glycogen, found in the liver, but in muscles in large amounts, is the carbohydrate which furnishes the energy for muscle contraction, when it breaks down into lactic acid. Cramer in 1926 reported one carcinoma of the breast that was characterized by cells containing glycogen. After 15 years of transplanting the tumor, it still furnished glycogen. Sodium iodoacetate prevents the formation of lactic acid in muscle.

Goldfeder, in studies with mono-iodo-acetic acid, treated 45 tumor-implanted mice. In 9, the tumors completely disappeared; while in 8, they diminished in size. Of 29 rats, 9 showed complete disappearance, and 6, diminution in size of the implants. The large, and especially the multiple, tumors increased in size and the disappearance occurred principally in the case of small tumors. The mono-iodo-acetic acid was injected, and the diet included supplemental calcium and ammonium chloride. Chlorides make iodine available in the blood also.

Sokoloff ran experiments which showed that lactic acid caused slowing down in the multiplication rate of ciliated protozoa, and also of yeast cells.

Then he investigated the action of lactic acid on tumorous rats and mice. While the lactic acid, fed in large quantities, did not affect the health of the animals, either control or experimental, it did inhibit the growth of transplanted sarcomas, and even brought about a complete disappearance of the tumors in some cases.

Sokoloff suggests that a combination of hydrochloric acid with lactic acid might be worthy of exploration in cancer. Guy and others have definitely linked *hydrochloric acid* therapy with cancer regressions in human cases. (See page 132.)

FATS

Since fats are related to certain vitamin effects, we shall consider them in both relationships. Fats, combined with iodine, prove important in the vitamin effects of cod liver oil on animals deficient in Vitamin A or Vitamin D, or both.

The ordinary *neutral fat* found in adipose tissue is easily mobilized during starvation, and is called "wandering fat" or "usable fat." The lipoidal fat found in epithelial cells of glands and elsewhere is usually "sessile" or "permanent."

The ordinary neutral fats are readily *reabsorbed* in starvation, while the lipoidal fats contain lecithin and other phospholipins which are more resistant to inanition. Lecithin (phosphorized fat) may be synthesized in the animal body.

Unsaturated fatty acids (lacking iodine) have been definitely identified with the anti-sterility vitamin called Vitamin E, and with the "essential unsaturated fatty acids" of Burr and Evans.

The highly unsaturated fatty acids are found in vegetable drying and semi-drying oils, and are present in the liver, heart and kidneys of mammals. They are notably present in the liver of codfish and sharks, which are being used much as a source of Vitamins A and D. Along with the unsaturated fatty acids, we find saturated fatty acids as well.

The best fish liver oils contain appreciable amounts of iodine, and their importance in curing several avitaminoses, as well as in goiter, depends on the fact that fats and iodine together will rapidly restore endocrine glands to normality, thus preventing losses of the essential vitamins, fats, and minerals, such as calcium, iron, and iodine.

Unsaturated fatty acids contain, at some point in the chain, one or more pairs of carbon atoms, united by a double union. This enables them to combine with *halogens* (iodine, chlorine, bromine) and so become saturated. It is possible to determine the number of double bonds of isolated acids, or of the whole combination as in cod liver oil.

The *iodine number* of unsaturated fatty acids is the number of centigrams of iodine absorbed by one gram of fat.

In diabetics who are unable to utilize fats properly, the percentage of lipoidal fats may rise from the normal value of less than 2% to

as much as 20%. Thus failure of the natural combustion of carbohydrates and fats together may permit fat and lipoidal increase in body fluids to a dangerous degree. We can see how preliminary *hyperthyroidism*, or the preliminary diabetic condition described by Shirlaw preceding cancer, may contribute to accumulations of sterols and phospholipids in cancers.

In passing we may mention the fact that at the University of Wisconsin investigators who induced tumors in laboratory animals with excessive amounts of ultra-violet light, furnishing Vitamin D, learned that the development of the "new growths" depended on the diet. Animals that had received diets high in fats developed cancers earlier than those on a low-fat diet. Fatty foods in excess cause such overactivity of the endocrine glands that the injurious action of excessive Vitamin D may be augmented. After glandular exhaustion, the normal amounts of protective elements would not be available to inactivate growth acids or to break down deposits of sterols common in cancers. It must be remembered that *fats* are also valuable in combination with iodine, in stabilizing the endocrines, and that they may offset iodine that is present in excess.

Dr. W. C. McCarty, Sr., of the Mayo Clinic, believes that *incomplete lipolysis* is a possible cause for continued stimulation to cellular hypertrophy and resultant cancer. "The products of lipoidal or hydrocarbon nature must be removed by certain mechanisms of the body or they continue such stimulation." McCarty stresses the fact that *carcinogenic substances* are closely related to the things that we call fat. Incomplete lipolysis may cause physical stimulation of regeneration with little or no differentiation, as seen in the initial stages of cancer. (*Proc. Staff Meetings, Mayo Clinic*, vol. 16, 1941.)

We interpret the "mechanisms controlling fat" as the endocrine reservoirs of iodine.

Stern and Willheim, "Biochemistry of Malignant Tumors," 1943, state, p. 830, "Investigations performed by the writers of this book suggested that the point of attack of the carcinolytic factors is to be seen in the lipid structure of the cancer cells.

Oike, to whose work with vitamins we shall presently refer, found that in rabbits a diet *high in fat*, regardless of its vitamin content, leads rapidly to carcinoma and death. This brings us appropri-

ately to consideration of the relationship between fats and glandular function.

H. Veldstra of Amsterdam, Holland, found that *irradiated fat*, like irradiated cholesterol, could be made carcinogenic. Such irradiation, which liberates iodine from fats and lipoids, might enable them to seize iodine, and thus to bring the tissue iodine down in such proportions as to cause tumor growth.

The other side of the picture is seen in the potency of "essential highly unsaturated fatty acids" in the normalization of the endocrine glands that control calcium and iodine in the body. Students of these essential fatty acids (some of whom name them as Vitamin F) have discovered that as *natural oils* they stabilize the endocrine glands, insure adequate calcium and iodine, and will offset excessive iodine. This is seen in the behavior of the highly unsaturated fatty acids in restoring sterility due to lack of the fats of Vitamin E. It is also evidenced in the extremely valuable use of cream and milk in the Sippy diet, given for gastric ulcer.

As we have shown, the attack on the mucous membranes of the digestive tract by excessive iodine and chlorine in the absence of fats, when hyperiodism in body fluids arises, is induced by the factors causing gastric ulcers. These include faulty diet, as in avitaminosis A, where fats are removed from the diet, and the thyroid becomes hyperactive, through minerals administered. Common causes in men are alcoholism, excessive smoking, worry, and fear. There were many cases of gastric ulcer after the Dunkirk evacuation. Fear causes pituitary and thyroid release of iodine. The administration of highly unsaturated fatty acids can function both to offset excessive iodine and to stabilize the endocrines which, overactivated, will permit the profoundly irritating action of iodine and chlorine on the digestive tract.

It has already been pointed out that fats transport and liberate iodine for effective use in the body. All these facts serve to emphasize the great importance of McCarrison's thesis on the fat-thyroid-iodine balance.

A law, set forth by General Sir Robert McCarrison of India in 1923, is called the "Fat-Thyroid-Iodine Balance." It was developed by McCarrison after experiments with pigeons in which he found

that inadequate absorption of iodine occurred when the food was contaminated. Cod liver oil, which restored the balance and normalized the animals, was found to contain 0.002% of iodine. The presence of saturated and unsaturated *fats and iodine together*, in cod liver oil, makes it superior to synthetic vitamins, in several "vitamin-deficiency" diseases, as the author has shown.

The pioneer in vitamin studies, Dr. Wilhelm Stepp, of Breslau, Germany, published in 1909 a report on bread and milk diet in animals which showed the link between essential fatty substances and health. Much research work on vitamins has been done since that time, and we cannot escape the overwhelming evidence that the natural fats are sources of vitamins and vital to the animal body.

Dr. Stepp is nutritional adviser to the German government. Taking his fundamental research and clinical work as a basis, the military rulers of Germany have robbed all of Europe, taking away *fats* and accentuating starvation by fiendish cruelties that bring glandular and mental exhaustion.

Cancers of the lungs and skin steadily increase in enslaved miners and munition workers of Europe. Cancers of the digestive tract will appear in agonized and starved millions. In them the old-age disease *cancer* will come prematurely.

The tremendous significance of the liver in the desaturation of *fats* has only recently been appreciated. When highly unsaturated fatty acids are fed, even more highly unsaturated ones may appear in the liver. Either added iodine or added *fats of highly unsaturated nature* will cause thyroid overactivity and induce greater storage of unsaturated fatty acids, and increased iodine, in the bile, and increased excretion of several essential minerals. There is of course considerable loss of iodine, calcium, iron, and vitamins during this hyperthyroidism. Nature strives always towards a bodily balance. When thyroid extract is fed, this desaturating process is speeded up, so that more and more of the highly unsaturated fatty acids are deposited in bodily storehouses. Increased amounts of the liberated iodine go in the bile to the small intestine, and pass to all cells and tissues of the body. Excessive accumulations of sterols and fats are broken down.

In his discussion of protective foods in the far North, Vilhjalmur Stefansson has emphasized the fact that he lived for 9 years on meat,

and that for 6 years he lived without *salt*. (See page 55.) The meat included the fats, together with essential minerals, in natural balance, since the animals eaten had derived their foods from the ocean. In a year's test, under conditions of civilization, and carefully supervised by Cornell University Medical School experts, Stefansson and a companion demonstrated their ability to remain in good health with meat as their sole diet. Here again they were careful to include the *fats* of their steaks. This test cannot be considered, therefore, as solely a demonstration of *protein* value, but indicates a balanced diet, with *proteins* and *fats* and *minerals*.

Krogh, of Denmark, studying the food-habits of the Greenland Eskimos, found that their diet contained about 50 grams of carbohydrates, 280 grams of protein, and 135 grams of fat. The seals, walruses, and whales furnishing this diet are all marine forms, and it is obvious that iodine would be present in protective amounts.

Natural sources of the essential highly unsaturated fatty acids are most likely to furnish them in proper combinations that will insure the normalized function of the endocrine glands.

"Let us a little permit Nature to take her own way:
she better understands her own affairs than we."

—MONTAIGNE

* * * *

ACID-PRODUCING AND BASE-PRODUCING DIETS

"What is food to one man may be fierce poison to others."

—LUCRETIUS, "De Rerum Naturae"

The efforts of nutrition workers to alter our diet so that vegetables and fruits predominate, have been so successful that these base-forming foods may jeopardize our health. If it is reasonable to believe the specious claims of advertisers, we all now need *their* kind of supplemental vitamins. Certainly the vegetarians find it regularly necessary to take cod liver oil, and to use plenty of milk and butter.

When the radio advertisers urge us all to indulge in expensive self-medication by means of "alkalizers," it is time to call a halt.

W. G. Evans (1938) and other physicians report that they are now having much more trouble with, and seeing more distress from, *alkalosis* than ever seen from *acidosis*. Advertisers conveniently neg-

lect to tell the public that the stomach is normally acid, and that hydrochloric acid is frequently administered by physicians to restore the necessary acidity. Without adequate hydrochloric acid and normal gastric enzymes, *undigested proteins* pass into the intestine and putrefaction occurs. Toxic effects are produced when such undigested proteins are absorbed into the body fluids.

Following the discovery that in *diabetes* there is a "ketosis" in which ketone bodies accumulate as products of incompletely oxidized fats, we have had an enormous wave of extremely questionable advertising about *acidosis*. The ketones consist of acetone, diacetic acid, and beta-oxybutyric acid, which are organic substances. This ketosis is a special kind of acidosis, but is not *true acidosis*, as pointed out by E. E. Ziegler.

It is with a great degree of pleasure that we are able to refer to a sane and well-ordered discussion of Dr. Ziegler's beliefs, as published in his booklet "Nutritional Origin of Cancer," which was privately issued at Boise, Idaho, in August 1934, and reached us September 22, 1934. Dr. Ziegler sent the book after receiving our own paper, "The endocrine glands in relation to cancer," which appeared in the July and August 1934 issues of the *Medical World*. We had evaluated the acidosis produced by fevers.

Dr. Ziegler has assembled much evidence in support of his thesis that cancer increase in civilized countries is due to the change in diets, which *now* consist largely of *base-forming foods*, replacing the original acid-forming ones.

He shows that *true alkalosis* is much easier to produce in a person than acidosis. "True acidosis rarely occurs except in starvation, and in acute fevers where the body tissues are undergoing rapid oxidation and catabolism." Ziegler shows that true acidosis is due to the excess of inorganic acid salts in the body, such as sulphates, phosphates, and chlorides. He deplores the "modern phobia of acidosis which has driven populations to alkaline self-medication."

He says, "Primitive man ate almost exclusively the acid-forming foods, meat, fish, birds, eggs and grain, and was relatively free from cancer and other alkalosis diseases that now affect civilization."

Ziegler has interpreted low cancer incidence in natives of Japan and Ceylon as due to their acid diets, which consist largely of rice,

marine fish, and seaweeds. He has not taken up the question of goiter-cancer relationships, or the iodine content of the foods from oceanic animals or plants, but he does state, "The mineral balance found in seafood is nearer to that of our requirements than other foods. From the standpoint of mineral-salt content, therefore, seafood is best adapted to human nutrition."

Ziegler inclines strongly towards the belief that *potassium* poisoning occurs in cancer. He cites Beebe and Clowes (see page 117) who demonstrated an excess of potassium and a deficiency of calcium in rapidly growing tumors, free from necrosis. The ingestion of base-forming foods is a factor in causing nutritional alkalosis, such as is present in cancer. Ziegler indicates how the beta-rays from radioactive potassium might stimulate abnormal cell-division and produce cancers. He states, "It is hypothesized that cancer is produced by nutritional alkalosis, and specifically by radioactive bases."

Miners who breathe traces of radioactive emanations in the cobalt mines of Schneeberg, Saxony, and of the neighboring Zoachimsthal have a very high cancer death rate. Over a period of three years, 71% of the deaths among these miners were due to cancer of the lung. (Wm. Boyd, "Surgical Pathology," 1942. W. B. Saunders Co., Phila.)

Ziegler believes that neoplastic diseases (cancer) are either somatic or germ cell mutations induced by traces of radioactive elements in the tissues. He believes that these radioactive bases are generally acquired from the environment in food or drink. Such traces of radioactive substances he believes to be taken up from the soil by the alkaline-ash foods, fruits and vegetables. He further states (personal communication, May 18, 1943) that cancer (cellular mutations) may be induced by a variety of agents in addition to radioactivity, and experimentally by carcinogenic chemicals.

Dr. S. P. Reimann (Lankenau Hospital, Philadelphia, Feb. 22, 1935) has brought out the fact that each undifferentiated cell in the body (adult as well as embryonic) has at least two possibilities of differentiation. "Normally, cell multiplication is brought to a close by the processes of differentiation, but more particularly *organization* of cells. Neoplasia occur since cells do not stop proliferating just because they have lost the capacity for properly differentiating and

organizing." Various degrees of loss in organizing property determine the tumor grading.

Reimann notes that when malignancy occurs there is an alteration in the potencies within the cells in the direction of both quantitative and, still more important, qualitative directions. This process has been called "*somatic mutation or change*." "Certain tumors of the internal secretory organs initiate changes identical in quality but increased in quantity from those initiated and controlled by the normal glands." (See page 164.)

Ziegler emphasizes the fact that along with the acid salts, *protein* must be supplied to restore the depleted cell-proteins, and to furnish amino-acids essential for the formation of hormones and enzymes needed to keep the metabolism normal. He recognizes the fact that toxic action on themselves of the decomposition products from proteins has been correctly interpreted by some cancer patients, who then avoid proteins. Deficiency in gastric secretion in cancer cases paves the way for their inability to digest proteins and subsequent actual distaste for meat.

The avoidance of proteins is not considered by Ziegler as a method of treatment for cancer. When adequate *hydrochloric acid* is present, the proteins will be digested properly. Hydrochloric acid will also produce the correct medium for adequate absorption of iron and calcium in the gastro-intestinal tract.

The Harvard group changed the acidity of the gastro-duodenal contents in anemias and found that iron was more potent in blood formation when absorbed from an *acid* rather than an alkaline medium. (Mettier and Minot, 1931.)

The absorption of calcium is readily accomplished from the upper, acid portions of the intestine. Alkaline media render calcium salts insoluble, as shown by Bernheim (1933).

We have referred to the work of Coley, using his combination of erysipelas and other bacterins (Coley's fluid) in cancer (page 41). We have also discussed Meyer's thesis on *acidosis* and the cure of cancer by fevers and other agents that induce such acidosis. Meyer treated a case of inoperable human cancer of the stomach with hydrochloric acid and cured it in about 4 months. (*Am. J. Surg.*, 15, 112, Jan. 1932.)

ALKALI-PRODUCING FOODS

FRUITS

Raisins
Muskmelons
Peaches
Pears
Currants
Oranges
Lemons
Bananas
Loganberries
Raspberries
Strawberries
Apples

VEGETABLES

Beans,
 lima
 string
 wax
 kidney
 white
Beets
Carrots
Spinach
Cucumbers
Celery
Lettuce
Rhubarb
Potatoes
Cauliflower
Cabbage
Radishes
Mushrooms
Rutabagas
Turnips
Water cress
Asparagus

NUTS

Almonds
Chestnuts

MILK

Cows' milk,
 whole
 condensed, unsweetened
Cream is almost neutral

ACID-PRODUCING FOODS

CRUSTACEA, FISH, SHELLFISH, MEATS

Lobsters
Shrimps
Oysters
Clams
Oceanic fish
Poultry, game birds
Rabbit
Beef
Veal
Lamb
Pork, lean

EGGS

Yolk
Whole eggs

CEREALS

Oatmeal
Rice
Corn, sweet
Bread,
 whole wheat
 white

FRUITS

Cranberries
Prunes
Plums

NUTS

Peanuts

These acid-producing foods have an alkaline ash, but their benzoic acid is changed to hippuric acid before excretion and body *acidity* is increased by them.

The *blood* under no circumstances becomes acid during life. The stomach *must* contain adequate hydrochloric acid for health. Hydrochloric acid facilitates protein digestion and the proper absorption of iron and calcium in the digestive tract.

Since hydrochloric acid and sodium chloride are both well known to pharmacists and physicians for their ability to cause the liberation of iodine from extracts, and also to induce similar changes making iodine available for new unions in the body (*halogen displacement law*), certain clinicians to whom the writer has furnished information on iodine have used hydrochloric acid alternately with iodides and report success in a variety of diseases.

Besides the pioneers, Drs. Burr Ferguson and W. B. Guy, long known for their hydrochloric acid therapy, a number of other physicians have described their success with HCl in medical journals. Colby, Salter, and Howell have been favorably situated for experimental as well as clinical work, and find HCl to be an extremely valuable medicament.

Ahlbohm has successfully used both hydrochloric acid and iron in the achlorhydric anemia of his precancerous cases. (See page 130.)

There is a great deal of uncertainty in the minds of people about just what the acid-forming and base-forming foods really are. So we include short lists of a few of the commonest ones.

CHAPTER VI

Vitamins

During the past 20 years remarkable progress has been made in the study of dietary deficiency diseases. Specific vitamins have been synthetically produced, and it has been possible to test the various vitamin-rich foods on cases of animal and human cancer. But results have been conflicting. This is not strange, for there has been a lack of knowledge on the part of vitamin students, and of cancer workers, regarding the relationship between vitamins and the glands of internal secretion. Moreover, some of the effects that have been attributed to vitamins are really due to the essential *minerals* and to the fats and lipoids in combination with them. Many widely advertised cereals are chiefly valuable because of the milk and cream that are added when they are eaten.

During the first World War, the lack of essential *fats*, *vitamins*, and *minerals* was felt in the European countries to an extent that influenced seriously the health of adults, children and the unborn. The pathological conditions that resulted have important bearing on the present World crisis, for subnormal children have grown up into men with mental twists, and without the stability that normal childhood might have insured.

In his study of 18,000 children during the Moscow famine period, Stefko found severe derangement of the thyroid, thymus, and reproductive glands. The chief factor was supposed to be vitamin deficiency although much of it was probably actual starvation of all foods.

During the war in Spain, 39 scientists in the United States arranged for the preparation and shipment to Madrid of 270,000 doses of nicotinic acid for the relief of the more than 40,000 people who suffered from pellagra. Optimists were made to realize, however, that this treatment meant only *temporary* relief. For the only real foods available to the pellagrans were those that had *caused* the dis-

ease, and the vitamin concentrates could not alone maintain their nutritive requirements. Just recently the Rockefeller survey in Spain has shown that children there suffer from *starvation*, not from vitamin deficiency alone.

The present European war presents the possibility of even greater hardship. Fear causes profound derangement of the glands of internal secretion, and starvation increases such disturbance, causing overactivity and speedy exhaustion of protective glands. Not only have the conquered neutral nations been subjected to the torture of bombardments and the agony of fear and humiliation, but they have been robbed of essential foods. The only persons on the continent that have been well fed are the *soldiers* of the invading armies.

A weapon that is all too powerful in the subjection of a nation is to take away its foodstuffs and cause bodily weakness, depression and despair. The only ray of hope is that after an extended period of starvation a revolution may be staged. Colonel Raymond Robbins once said: "A man will lie, after being hungry for 24 hours; he will steal, after 48 hours; and he will kill, after being starved for 72 hours."

In discussing the vitamins, we shall show how they aid in preserving the normal function of protective glands of internal secretion. We shall also emphasize the possibility that *excessive dosage* with some of the vitamin concentrates may cause serious derangement of glandular function and actually induce *cancer*.

The remarkable modern advance in nutritional science has come as a result of the evaluation of vitamins, and the physician has a truly wonderful array of potent preparations to give to the persons who suffer from vitamin lack. In general, we must acknowledge that such vitamin deficiencies are *multiple*, however, and that actual starvation occurs. We know that some vitamin concentrates are *too potent* and extremely injurious.

It is unfortunate that some high-pressure advertisers of vitamins and hormones have prejudiced medical men by their extravagant claims.

The truth about vitamins is more remarkable than the assertions of advertisers. For the activation and perfect function of the *glands* of the body is determined by the basic foodstuffs, and vitamin students

are responsible for cleancut evidence which emphasizes the effects of *glandular disorders*. More than 25 years ago, Sir Arthur Keith in his "Engines of the Human Body" discussed vitamin-gland relations. This writer has corresponded with him on vitamin-gland balance.

The enormous increase in young children of diabetes, anemia, infantile paralysis, arteriosclerosis, and *cancer* has been linked, clinically and experimentally, with glandular disturbance or exhaustion. All of these diseases are related to improperly functioning glands of the body.

Today, with all of our publicized information about diet and vitamins, there are more cases of imbecility and cretinism resulting from goiter in this country than at any time in the nation's history. Since the depression, efforts to prevent goiter have fallen off. In the great goiter belt, it is stated that $\frac{1}{5}$ of the boys and $\frac{4}{5}$ of the girls have goiter. And *glandular disturbance* is produced by lack in essential vitamins, while the administration of some types of food will hasten its appearance.

In his editorial, Dr. G. C. Engel (1943), discussing the dangers of *thyroid adenoma*, emphasizes the fact that adenomatous or nodular goiters are potential cases of carcinoma. In Engel's practice, 90.9% of his cases of thyroid carcinoma had their origin in adenomas of the thyroid. He cites the report of F. A. Collier that 80% of patients autopsied in a goiter belt had adenomas (nodules) of their thyroid. Endemic goiter paves the way for adenomas.

There is a very suggestive report by A. Ciocco (Nat. Acad. Sci., 1940) on the death rate of 2571 married couples who died in a Maryland county between 1898 and 1938. They tended to have the same length of life or vitality, as shown by the fact that when either the husband or wife died of cancer, heart disease, or certain respiratory diseases, the other spouse died of the same disease, in a preponderance of cases. Selection of a husband or wife of the same constitutional type and identity of environment and living conditions are named as causes by Ciocco.

Glandular makeup would answer both these conditions favoring the development of diseases due to lower resistance to cancer. Nutritional deficiency would affect the glandular function, for vitamins are needed to insure endocrine normality.

VITAMIN A

When animals are placed on a Vitamin A-free diet, the thyroid and other associated glands are at first overactivated. This is due, as the author first pointed out in published reports, to the fact that the salt mixtures given contain various elements, including iodine and chlorides, which in the absence of fats cause typical goiter. Students of Vitamin A deficiency remove *fats* from the diet. Gastric ulcers, which appear early in the stages of Vitamin A deficiency, are associated with thyroid overactivity. Vitamin A deficiency or fat deficiency

FOOD SOURCES OF VITAMIN A

<i>Excellent</i>	<i>Good</i>	<i>Fair</i>
Cheese	Eggs	Cottage cheese
American	Duck	Fish
Cheddar	Hen	Haddock
Cream	Fish	Pollock
Limburger	Herring	Salmon, canned
Swiss	Eel	Codfish
Whole, raw milk	Beef	Shellfish
Egg yolk	Heart	Clams
Butter	Kidney	Oysters
Cream	Liver	Beef
Liver	Fish roe	Pig liver
Calf	Herring	
Lamb	Cod	
Fish liver oils	Avocados	
Shark	Bananas	
Salmon	Cherries	
Halibut	Cantaloupe	
Sardine	Pineapples	
Cod	Cabbage, green leaves	
Asparagus	Dandelion greens	
Carrots, raw	Hubbard squash	
Chard	Escarole	
Kale	Lettuce	
Turnip greens	Peas	
Sweet potatoes	Parsley	
Spinach	Tomatoes, raw	
Apricots		
Yellow peaches		
Prunes, dried		

will permit hyperthyroidism and subsequent injury by iodine-chlorine combinations in the stomach and upper duodenum.

Tashiro and Schmidt, in 1931, showed that thyroid feeding increased the susceptibility of guinea pigs to bile salts, which cause gastric ulcers. They designate thyroid overactivity as one of the most aggravating conditions favoring gastric ulcer. In our own publications we have shown how fear, worry, fat or vitamin starvation, and alcoholism, all induce gastric ulcers.

In his statistical study of diseases since 1924, Percy Stocks has discussed the fact that cancer is extremely common in goitrous regions. He has also correlated tuberculosis, a high rate of maternal mortality, and gastric cancer, all found in the same region. Susceptibility to respiratory diseases is associated with Vitamin A deficiency, and also with glandular derangement. Charles Mayo has pointed out the fact that high mortality of women during *pregnancy* is associated with thyroid disease.

Dryness of the skin is seen in animals on a Vitamin A-deficient diet, and Pallotti, in 1935, reported from a study of the skins of rats killed one each month. Examination of the skins showed a gradual increase in hardening, until, at the end of 8 months, an actual skin cancer had developed.

In 1916, McCarrison learned that pigeons developed epithelial tumors, or "new growths," when on a diet lacking in vitamins. He compared this with the disturbed condition of the mucous coat of the stomach in Pappenheimer's rats on low vitamins. He also recorded a similar growth in the monkey.

In 1927, Fujimaki induced cancerous changes in the stomach of rats with a Vitamin A-deficient diet. Similar results were obtained when heated olive oil was added to the diet, and carcinomatous growths developed in the upper end of the stomach in rats. The cancerous growths resembled those recorded earlier by Fibiger, and also by Yogagawa. In one case, nodules that had migrated were found in the lung also. Fibiger's cases developed after a dietary deficiency and the invasion of parasites, together.

Rhoda Erdman and associates (1927) fed a diet lacking Vitamin A to rats, and induced tumors in the mammary glands after 7 months.

Oike, in 1930, reported to Japanese Pathological Society that

Vitamins A and B in excess in the diet prevented tar cancer from developing in rabbits.

Montrose Burrows, in a series of papers beginning in 1926, has stressed the fact that poor dietary, and a drop in general nutrition, favor the development of human cancers. He found that operations and X-ray treatment were relatively ineffective in cases where the general bodily condition could not be improved. The cancers recurred quickly.

Testing with animals, Burrows and associates have learned that in rats on a diet low in Vitamin A typical precancerous changes were secured more readily by a single application of coal tar or by X-rays than they were by repeated applications in well-nourished rats. He also noted that coal-tar treatment caused rapid depletion of Vitamin A in the rat. A general effect on the lymphoid tissue and on the digestive organs is characteristic of vitamin deficiencies and of tarred or radiated animals.

As this author has shown, the agents that induce thyroid overactivity will deplete animals and human cases of Vitamin A. And, with the application of coal tar, or the experimental use of X-rays or of sunlight, there ensues greatly increased defensive activity of the glands of internal secretion.

Tipper, in his book, "The Cradle of the World, and Cancer," reports that during 20 years of service in Africa among the Bene, a Nigerian tribe comprising 2 millions, he saw no cases of cancer. He says, "The equator is the cradle of the World, and amongst the race of which I write, where civilization is absent, and the food is perfectly natural, and abundant; where the natives have never lost touch with the first principles of feeding, and there is no such thing as constipation, there is no cancer." With *natural foods*, the glands of internal secretion are well balanced, and there is no intestinal stasis. Moreover, Tipper's reports show that the natives regularly consume each day about 4 ounces of red palm oil. The *Indian Research Bulletin* cites red palm oil as furnishing 50,000 units of *Vitamin A* in the daily intake named.

Sugiura and Benedict, who tested cod liver oil, olive oil, linseed oil and chaulmoogra oil at a level of 10%, found that in rodents there was no effect on the growth of the Flexner-Jobling carcinoma nor the

rat sarcoma. On the other hand, Freund and associates learned that diets rich in *olein* conferred refractoriness to inoculation with carcinoma and decreased the growth of rat carcinoma already established.

When Kuh, in 1932, repeated the experiments of Sugiura with cod liver oil, he found that implants of the Twort mouse carcinoma were not affected by this type of Vitamin A, in an amount of 500 Vitamin A units. But when he tried maximal doses—1000 or more units of the "provitamin," carotene, the tumors were in some cases retarded, or inhibited. Kuh attributed the effects to carotene, after it had been transformed in the liver into Vitamin A. But the complete Vitamin A includes iodine; and carotene with thyroxin has been shown by Von Euler to maintain the equilibrium in the thyroid gland. Again, we may relate the thyroid to protection against cancer growth. For stabilization of the glands that control *iodine* and *calcium* will insure the availability of two of our best known elements that will break down cancers and prevent their development.

Thomas, in his experiments with carotene, was able to induce more rapid calcification of tumors in experimental animals (1932). Here, the action on iodine reservoirs, which control calcium distribution, was probably exhibited, as in other "unsaturated" substances that balance glands.

Liver extract has been used by Douglas-Webster of Middlesex Hospital, London, as intramuscular injections to relieve radium sickness. Anderson has augmented such liver extracts with iron and Vitamin B as well.

In 1928, this writer used iodide of iron (ferrous iodide) in extremely minute doses, in tests with rats on a Vitamin A-free diet. The experiments were run primarily to determine the relationship of iodine to the signs of glandular disturbance in vitamin-deficient animals. The fact that ferrous iodide tended to offset injurious effects of Vitamin D was not appreciated until later. It was with gratification that we learned that Quimby, in 1922, had recommended iodine to X-ray operators to offset radiant energy injuries. Our own experimental work with iodine and Vitamin A-deficient animals was supported by the study of Wendt, who, in 1935, *corrected thyroid overactivity* and thus induced a return of *Vitamin A* to the blood of goitrous (hyperthyroid) patients. The most valuable contribution

to our knowledge of how to offset sun injury (and radiant energy) has been made by H. Eder of California. Dr. Eder, since 1930, has reported his success in cases of excessive sun exposure by an iron compound in cod liver oil. This furnishes Vitamin A, iron, iodine, calcium and the *fats* which facilitate proper assimilation of calcium. Radiant energy in excess activates iodine, and through heavy glandular stimulation causes extensive losses of calcium, with its bound iron. These elements *must* be speedily restored.

Cancer patients, not irradiated, continually lose large amounts of calcium, iron, and iodine, as well as other elements. Their glands are in defense, but the cancers ordinarily grow, drawing from the body of the host, just as a baby grows. In pregnancy, many human cases of cancer and experimental animals alike demonstrate the fact that the cancers will grow more rapidly than in non-pregnant cases. We shall discuss the reason for this under the section on chemical agents involved in cancer growth (page 204). Suffice it to state here that without adequately functioning endocrines in the mother, a human fetus may develop abnormally.

Growing tumors have a very great Vitamin A content, according to Vogt's report in 1932. (Vogt, E., *Med. klin.*, 28, 1344-1345, 1932.) We know also that tumors contain small amounts of iodine when they are most rapidly growing, but that those that are breaking down and regressing contain extremely large amounts of iodine. (Holler, 1923, see page 137.)

Maisin reports that fresh liver and fats have a growth-promoting effect on experimental cancers. This we attribute to the fats, the fatlike cholesterol, and the amino-acids in liver which actually *feed* the growing tumors. Iodine in the liver would be guarded by these growth substances, and would also accelerate growth of the tumors, which demand small amounts of it, just as do young seeds, in their growth.

Liver extracts have proved *beneficial* in human cancer (page 76). When Maisin extracted liver with ether in 1939 studies, he secured from it a growth-inhibiting substance. This consisted of the very elements which, likewise extractable from growing cancers, are able, when injected in a state where they can act without the previously antagonizing and limiting substances, to break down tumors. Ex-

tracts from the breasts in a condition of mastitis (inflammation); fluids from a Rous chick sarcoma, and extracts from mammary cancers have all proved effective in causing regressions of such growths. We have conclusive evidence that small amounts of some elements will hasten growth, while larger amounts will prevent proliferation of cells in tissue cultures. Iodine is here the key element.

In 1913, Alexis Carrel, of the Rockefeller Institute for Medical Research, was able to accelerate the growth of fragments of the hearts of embryonic chicks in *tissue cultures* with extracts from chick embryos, spleen, kidney, muscle of the adult chicken, the Rous sarcoma, the thyroid gland.

In 1930, Sato found that thyroxin (65% iodine) in a 1 to 500,000 dilution stimulated the growth of in-vitro chick myxosarcoma (muscle cancer). In a 1 to 100,000 dilution it stimulated growth of cultivated chick heart.

McCarrison, in 1933, was able to accelerate in different degrees, according to the concentration of sodium iodide used, the growth of various tissue cultures, including the thyroid gland.

Rapid regression in the growth of experimental and human cancers has been secured by iodine, and by extracts containing it. (See pages 136-138.) We have also reported the action of iodine, unguarded by fatty acids, in causing the actual re-absorption of young embryos (page 116). We have elsewhere reported in numerous articles (since 1934) that such iodine action may furnish the key to glandular and vitamin therapy in cancer.

By stabilizing the iodine reservoirs (see Wendt, page 79) and insuring adequate iodine in the body fluids, Vitamin A-rich foods will facilitate the emergency use of iodine, whenever it is needed to prevent excessive cell-growth. Such abnormal and excessive cell-growth is facilitated by the presence of amino-acids, fatty acids, and lipoids that lack iodine.

VITAMIN B₁

Vitamin B₁ deficiency is classically linked with the disease known in birds as polyneuritis, and in humans as beri-beri, which develops when they are fed polished rice, instead of the natural *whole* brown rice. In China, the human disease was known as early as 2600 B.C.

FOOD SOURCES OF VITAMIN B₁

<i>Excellent</i>	<i>Good</i>	<i>Fair</i>
Milk, whole raw	Sweetbreads	Oysters
Yeast, moist	Brown rice	Beef liver
Lean pork	Rye	Lean beef
Soybeans, yellow	Wheat	Eggs
Wheat germ	Oats	Egg yolk
Peanuts	Asparagus	Spinach
	Carrots	Cabbage
	Mushrooms	Rutabagas
	Radishes	Potatoes
	Lettuce	Sweet potatoes
	Raw tomatoes	Orange and juice
	Almonds	Bananas
	Chestnuts	
	Cocoanuts	

Not only do the coverings of grains contain Vitamin B₁ but the germ is also rich in it. In fact, wheat germ is now classed with yeast as a commercial source of it. The outer layers of grains and seeds contain the preponderance of iodine, which is present in wheat germ as well.*

Lack of appetite is one of the first symptoms of Vitamin B deficiency. Animals fail to grow, become emaciated, and finally lose the use of their hind limbs. At first it was believed that the nervous symptoms were the chief one, hence the name *polyneuritis*.

The pathology of the nerves is centered in the *myelin sheaths*, which consist of semi-liquid fatty material. This substance is rapidly broken down when beri-beri develops. It is rapidly restored when doses of the vitamin are administered.

In early stages of beri-beri, there is diarrhea and colitis. The great overactivity of the endocrines in early stages of Vitamin B₁

* In his book, "England and the Farmer," Doctor L. J. Picton says, "The modern dietary, often from fastidiousness, is arbitrarily selective: the germ and bran robbed from the grain and with them the fertility influence, the nerve food, and the neuromuscular tonic; the peel and core of the apple discarded, and with them the ascorbic acid and the iodine; the outer layers of the potato pared off, and with them the most of the albumen, iron and manganese, to say nothing of the sapid substances which make potatoes in Ireland memorable. The palate of a child informs him of the difference: 'How are the triplets?' 'Well, sir, those two are all right, but Ernie here is off his food.' 'How?' 'Well, he won't eat his potatoes, but he'll eat the hen's potatoes!'"

deficiency causes heavy losses of calcium, creatin and iodine from the muscles, and general muscular weakness develops.

Later, there is atrophy of the liver, kidneys, spleen, pancreas, thymus and thyroid glands. Reduction in the amount of iodine in body fluids permits lipoids to increase in the adrenal (suprarenal) glands.

Blood iodine is remarkably high in *early* stages of Vitamin B₁ deficiency. Our interpretation of the glandular changes and the condition of the nerves is that in the absence of the *iodine* that normally is found in the seed coats, the remaining starches and fats of the seeds demand iodine and cause great overactivity of the glands. The muscles and the endocrine glands are storehouses of a large proportion of the body iodine. When vast amounts of iodine are liberated into the body fluids, the direct action of this on the lipoids and fats is seen in the rapid breaking down of the myelin sheaths of the nerves and the disintegration of the fats and lipoids of nerves and nerve endings. Body fat is rapidly lost as well.

The late stages of beri-beri and polyneuritis with the typical *edema* and the before-mentioned atrophy of the glands, characterize the inability of the patient to control body fluids and mineral metabolism. Muscle weakness is associated with *glandular exhaustion*, after the overactivity that has caused losses of the minerals needed for muscle contraction (calcium, creatin, iodine). Abelin found that the *thyroxin* content of the thyroids of animals depleted of Vitamin B₁ is less than normal, and that thyroid-iodine is restored to normality after administration of Vitamin B₁-rich diets. This indicates stabilization of glandular function.

When Vitamin B₁ is administered to depleted animals, in proper amounts, the adrenal cortex loses much of its lipoids, and Nissl granules reappear in the nerve cells. Paralysis disappears. These conditions may all be identified with the normalization in function in the glands that control lipoids, fats, calcium, iodine and other elements.

The first instance of the use of glandular extracts in vitamin deficiency, except of course the classic cod liver oil, was seen when Dutcher, in 1919, reported beneficial effects on pigeons with polyneuritis, when he fed them thyroid extract. He also used pituitary extract in similar tests, and relieved the paralysis. (*J. Biol. Chem.*, 1919, 39, 63-.) Since, as we have shown (Chidester, F. E., *Archiv.*

int. de Pharmacodynamie et de Thérapie, 1934, vol. 48, Fasc. III et IV, pp. 354-365, 1934), iodine is found in large amounts in the anterior lobe of the pituitary, the effects of iodine were presumably manifested by both extracts.

Swoboda, in 1920, tested the Vitamin B content of various glands, and found that it was present in appreciable amounts in pineal, pituitary, testes, liver, kidney, and thyroid. (*J. Biol. Chem.*, 1920, 44, 531-.)

In 1920, Seaman not only cured polyneuritic pigeons with thyroid extract, but he learned that such extracts were effective in causing the rapid metamorphosis in tadpoles characteristically induced by iodine.

In 1927, Pighini found that polyneuritic pigeons furnished thyroid glands that were so low in iodine that tadpole metamorphosis did not occur when they were fed, while the thyroids of normal pigeons caused marked acceleration in the speed of metamorphosis of tadpoles.

Ariyama, in 1932, reported on his successful use of sodium iodide hypodermically, and thyroxin orally, to check neuritic symptoms produced by diets free from Vitamin B. Ridley was able to treat beri-beri successfully with tincture of iodine (1925) and Shimazano used *thyroid extract* in late stages of beri-beri. He found (as we might expect) that in the *initial stages* iodine and thyroid extract exaggerated the signs of beri-beri.

Von Eulenberg-Wiener states that *adrenal cortex* extract has proved successful in lessening symptoms of polyneuritis and beri-beri. Eskin has shown that adrenal cortex markedly accelerates the metamorphosis of tadpoles, as does thyroid extract or iodine. It is evident that, in late stages of avitaminosis B, iodine or iodine-rich glandular extracts will aid in restoring physiological balance.

Vitamin B₁ is also extremely valuable in offsetting the injurious effects of excessive Vitamin D, which are so severe when Vitamin A is low or lacking. It is possible to conclude that this *protective action* is in part due to the conservation in the body of iron and iodine, both of which are known to be valuable in offsetting sun injury and radiant energy effects. For the writer has shown (1928) how ferrous iodide seems to offset somewhat the injurious effects of excessive Vitamin D, or ultraviolet exposure, and Eder (1930) has used ferrous carbonate and cod liver oil (iodine-rich) in the treatment of sun injury in children (page 80).

In the treatment of "radiation sickness" of cancer patients a number of clinicians have used combinations of Vitamin B and iron with brilliant results.

In 1930, Oike reported that Vitamin B deficiency favored the development of *cancer* in rabbits treated with tar. Experiments by Dahldorf in 1932 indicated that deficiency in Vitamin B permitted the development of gastric ulcers in albino rats. Such gastric ulcers could eventually develop into gastric cancers. In a number of vitamin deficiencies, the thyroid gland becomes overactive, and *irritation* by iodine and chlorine in the digestive tract gives rise to degenerated mucous membranes, and ulcers.

Vitamin B feeding tended to offset the beneficial effects of Vitamin A, in experiments with cancerous rats reported by Montrose Burrows. It is difficult to determine why this occurred, but it is quite possible that at certain stages in cancer development the Vitamin B might prove disturbing to animals that approached physiological equilibrium, after Vitamin A had been given. For Vitamin B requirements are very high in hyperthyroidism, and there is antagonism between thyroxin and Vitamin B. In experiments where Vitamin A-deficient rats were given cod liver oil, Norris and Church found that it was necessary to furnish from 15% to 18% of Vitamin B, instead of from 5% to 8%, as some workers did. Cancerous animals suffer from hyperthyroidism, but in advanced stages the glands do not furnish iodine.

Funk learned that deficiency in Vitamin B caused slower growth in the Rous chick sarcoma. Our interpretation of this condition is that there might be a temporary effect as in short fasts, such that the hydrocarbons and fats of Vitamin B would not be present, and the protective glands would become overactive, distributing large amounts of carcinolytic elements which might act to break down cancers. In general, it seems that such an effect would be only transitory, for stimulation of iodine reservoirs will ultimately lead to their exhaustion, unless adequate elements are furnished to satisfy the need for new supplies.

In studies of precancerous mouth lesions and mouth cancer, Martin and Koop (1942) of the Memorial Hospital, N. Y., found that the average weekly intake of Vitamin B complex was low. They

were able to induce normal mouth conditions in some cases. Yeast seemed valuable. They advocate the routine use of supplemental Vitamin B therapy in mouth cancer.

Preparations of Vitamin B₁ have been used with success in the treatment of infantile paralysis, and reported by Stern to benefit *cancer*, as well as proving valuable in nerve disease. The fact that injections of Vitamin B₁ stimulate the sympathetic nervous system and the thyroid gland is suggestive of their mode of action in these diseases.

In vitamin studies, it is well known that adequate Vitamin B will guard against excessive overactivity of the thyroid gland, and thus prevent premature exhaustion of the glands. It could also prevent the *gastric ulcers* which arise from irritation by iodine. It augments Vitamin A supplies, in cases of profound depletion, and attempted restoration by cod liver oil.

Dr. D. T. Quigley in his "National Malnutrition" (1943) has shown that in toxic conditions of the thyroid the increasing metabolism burns up Vitamin B₁, and that this vitamin should be furnished, along with iodine, balancing minerals, and other vitamins.

He also cites Mills (*Jour. A. M. A.*, May 3, 1941) who described a case in which a woman of 47 developed signs resembling those of over-dosage with *thyroid extract* after she had taken large doses of vitamin B₁. Increased activity of the thyroid was produced by Vitamin B from yeast, in tests made by Sandburg and Holly. (*J. Biol. Chem.*, 1933, 547-.)

Vitamin and mineral balances are necessary in diseases that induce thyroid and other endocrine overactivity. Cancer induces such hyperfunction, and is marked by losses in minerals and vitamins.

VITAMIN C

Manifestations of scurvy, which is due to lack of Vitamin C, include diarrhea, loss of weight, anemia, swollen gums, and necrotic areas in the jawbone. Teeth may fall out and bones become very fragile.

Vitamin C is found in all fresh fruits and tubers, citrus fruits, tomatoes, and wild rose seed-pods (hips), the last named being in

FOOD SOURCES OF VITAMIN C

<i>Excellent</i>	<i>Good</i>	<i>Fair</i>
Grapefruit and juice	Whole milk	Asparagus
Lemon and juice	Condensed milk	Green beans
Orange and juice	Pineapples	Celery
Spinach, raw	Limes and juice	Rhubarb
Rutabagas	Potatoes	
Beet greens	Sweet potatoes	
Cabbage, green leaves	Cantaloupe	
Broccoli	Apples	
Peppers, red, green	Peaches, raw	
Strawberries	Beef liver	
Water cress	Cauliflower	
	Tomatoes	
	Peas, green	
	Bananas	
	Cranberries	
	Radish	
	Pumpkin	

use today in Britain, because of the difficulty in securing fresh fruits and vegetables.

Ascorbic acid is most abundant in the glandular tissues of animals, but *beef liver* is the only one of such glands commonly eaten. The largest amounts of Vitamin C have been found in the anterior pituitary, the corpus luteum (yellow body) of the ovaries, and the adrenal glands. In fact the adrenal glands were used as the source of the first *crystalline* Vitamin C, in 1930.

There is an intimate relationship between the thyroid gland and Vitamin C. General Sir Robert McCarrison found that in scurvy there is a great concentration of iodine in the thyroid gland. Thyroidectomy causes a temporary increase in the Vitamin C of the adrenals. By heavy dosage with thyroid extract or thyroxin, Mosonyi produced in guinea-pigs marked hyperthyroidism and diminished Vitamin C in the adrenals.

Paal has shown that in rats the thyretropic hormone of the pituitary gland and thyroxin both produce an increase of 256% in the concentration of the antiscorvy vitamin in the *adrenal glands* and the kidneys. We know that in extreme scurvy the adrenal lipoids in-

crease and the calcium and phosphorus disappear from those glands. All these conditions suggest at once that *normalization* of the thyroid gland will aid in conserving Vitamin C. Lemon juice influences favorably the deposition of *calcium*.

Pasteurization of milk destroys its Vitamin C and drives off as much as 83% of its iodine. Raw cabbage, which prevents goiter in rabbits, contains Vitamin C. When cooked it has lost its antiscorbutic properties, and it then produces goiter since it is desaturated of volatile iodine. This naturally leads us to consider the fact that potent natural Vitamin C extracts were shown by Daubney in 1926 to contain *iodine*. Heyl has secured all the physiological and histological effects of the thyrotropic hormone of the pituitary on the *thyroid* gland by administering pure "ascorbic acid," the commercial anti-scurvy vitamin.

The experiments of Woodhouse with ascorbic acid in tumors have presented a new viewpoint as regards the rôle of lactic acid, which has long been considered to be a stimulus for growths. Since lactic acid is oxidized by Vitamin C, he expected to find that the injection of ascorbic acid into the tumors would decrease lactic acid present and cause tumor growth to cease. But the injection of Vitamin C actually *stimulated* the multiplication of cells in the tumors. Woodhouse therefore concludes that lactic acid has an inhibiting effect on the growth of cancers. (This is in opposition to evidence given on page 61.) (See Woodhouse, *Biochemical Journal*, 1934, vol. 28, p. 1974.)

This writer suggests that since the chemical balance of a tumor is so delicate, here may be another instance of the temporary binding (by injected vitamin C) of certain of the inhibiting elements present. For one of the tests used to determine Vitamin C is an iodine test.*

The fact that Vitamin C deficiency favors the development of gastric ulcers is well known. And gastric ulcers may develop into cancers.

The similarity in action of ascorbic acid to the thyrotropic hormone of the pituitary and the well-known rôle of Vitamin C in normalizing the thyroid function seem to justify use of tomatoes, lemons

* Szent-Gyorgyi (*Biochem. J.*, 22 (2), 1387-1409, 1928) has shown that the iodine-reducing substance in orange juice largely consists of hexuronic acid Vitamin C.

and oranges in cancerous cases. At Memorial Hospital, Vitamin C administration reduced experimental cancer (1943).

VITAMIN D

Vitamin D regulates the absorption and utilization of calcium and phosphorus, which is laid down in the form of calcium phosphate, to form bones. The term *rickets* comes from the old English word "wrikken," meaning to twist or bend, and refers to the softness of the bones. Rickets was common among prematurely born children, but until the days of proprietary foods, and modified cow's milk, was rare in the sections where nursing mothers had an adequate diet. Rickets may occur in breast-fed babies, as in Manchuria, in 1924, where mothers were starving.

Rickets affects the whole body of the child. The muscles are weak, the head rolls about, and the bones are slow to harden. The legs become bowed or knock-kneed, and pigeon-breast deformities occur. Various curvatures may develop. Anemia, convulsions and nervousness may appear.

Experimental studies have shown that rickets may follow heavy dosage with pituitary hormone, while Telford Smith recorded its development after thyroid administration to cretinous children.

Characteristic in the experiments of Murray (1923) and Thompson (1932) were overactive thyroid glands in animals on rachitic diets. Our own experimental rickets in fowls (*Int. Clin.*, 1934) was the result of the injection intravenously of "antuitrin S," which produced hyperactivity of the thyroid gland. Such thyroid overactivity

FOOD SOURCES OF VITAMIN D

<i>Excellent</i>	<i>Good</i>	<i>Fair</i>
Egg yolk	Butter	Clams
Liver	Eggs	Oysters
Beef	Marine fish	
Chicken	Salmon	
Pork	Mackerel	
Fish liver oils	Sardine	
Irradiated milk	Milk, from summer pasture	

has been reported by Aub to induce a 250% increase in losses of calcium.

Long before any exact knowledge of the control of the disease "rickets" existed, fishing folk used cod liver oil in the treatment of rickets, and also in joint affections of old age. They rubbed it on and used it internally. Natural cod liver oil is rich in iodine, fatty acids and sterols, and normalizes thyroid activity. Today we know that cod liver oil is superior to most anti-rachitic remedies, because it contains Vitamin A, and also furnishes iodine which is important in the regulation of calcium distribution and offsets excess radiation.

The fact that *bile* contains *iodine* which the liver has released in its process of desaturating fats may be significant, for experimental studies (Greaves) have shown that in the absence of *bile*, Vitamin D is not absorbed from the intestine. Not only is bile rich in iodine, but we know from the work of Hanzlik (1928) that iodides benefit animals on a rickets-producing diet. Nitschke (1925) injected thyroxin and healed rachitic rats.

For thousands of years, *sunlight* has been used by primitive peoples to cure numerous diseases, including scrofula, rheumatism, and *rickets*. The ancients who worshipped the "Sun God" were no more assiduous than some of our modern devotees to sun bathing. In moderation, sun bathing is justified, for we have evidence that the ultra-violet rays increase the blood content of *iron* and make available the *iodine* of the body. The adequate distribution of *calcium* and other essential elements is facilitated, increased oxygen goes to the cells, and glandular function is coordinated. But there is distinct danger from *excessive* sun exposure, and from the researches of Melanby and Green (1928) we know that high Vitamin D and *no* Vitamin A causes rapid appearance of abscesses of the glands and permits infections to appear in the digestive system, respiratory tract and reproductive and urinary organs. Keratoses of tissues appear, and signs of Vitamin A deficiency are hastened. Thus cancer may develop.

Irradiated ergosterol and cholesterol have been in use for some years added to cod liver oil and even to milk, in order to step up the Vitamin D. Irradiated foods have been patented. But A. Morgan, Daniels, and others have proved that Vitamin D, without considerable

guarding Vitamin A, is most injurious. Normally, cod liver oil of the most potency in both Vitamin A and Vitamin D has considerable iodine. And inorganic or organic iodine will protect animals against the injurious action of irradiated sterols. Organic iodine is superior in preventing scleroses due to ergosterol, or to cholesterol. Thus cod liver oil, without any addition of irradiated sterols, is a safe source of Vitamin D.

Alvarez, of the Mayo Clinic, noting the reports of careful workers on the toxicity of Vitamin D to children, says, "I have been worried over the published reports of children dying with signs of injury due to an excessive intake of Vitamin D." He has indicted that "great army of propagandists who quote any scripture they can find to serve their purpose, which is to frighten people into buying their particular 'health food.'"

In 1774, Fauré reported (Paris) on the use of sunlight to heal wounds, remove scars and tumors. In 1778 he reported cures of ulcers and cancer of the lip, cured by sunlight.

In advancing the theory that certain cancers may develop from *insufficient* Vitamin D (and possibly lack of Vitamin A), Dr. Frank Apperly (1942) directs attention to those areas receiving much sunshine where cancer mortality decreases. Since we know that Revillet cured congenital myxedema in children by sending them to the Riviera, where they received sunbaths, this links with our general thesis on glandular function and health. Moreover ultra-violet light has been used successfully in goiter by Swiss physicians.

A moderate amount of irradiation causes a release of iodine from bodily storehouses, and is beneficial, but excessive sun exposure may cause glandular exhaustion. Vitamin A is protective against excessive Vitamin D, as previously indicated.

The cancer-inducing action of too much sunlight has been stressed by Watkins-Pitchford, James Ewing, and Roffo.

Andrews of Presbyterian Hospital, New York, has recently (1942) suggested that the so-called "smoker's cancer" of the lower lips of laborers may be due to chronic inflammation from habitual sunburn, and not to smoking.

In her experiments in 1928, Erdmann used 80 rats, receiving Vitamins B and D only, with no Vitamin A. In this group, four developed tumors.

Roffo's investigations deserve especial mention, in view of the fad for oversunning, which so jeopardizes the health of children. In 1935, Roffo (Buenos Aires) reported on his experiments with a set of 150 white rats, given ultra-violet irradiation for stated times, each day. All developed tumors. Later he ran tests with 410 white rats, exposed to the sun for 6 hours daily, over a period of 11 months. Of these, 52% showed tumorous growths in the skin, associated with increased cholesterol. (See page 109.)

Not only do we have evidence from Roffo regarding the injurious action of ultra-violet light and the sun, but it is well known to all vitamin students, that Vitamin D, unguarded by adequate amounts of Vitamin A, will cause greatly over-activated glands of internal secretion. Prematurely exhausted, these glands permit many signs of old age, including degeneration of the heart and hardenings of the tissues in the respiratory, digestive, and reproductive tracts. Gallstones, cataracts, and arterioscleroses appear as manifestations of glandular exhaustion, and accumulated cholesterol. We have already mentioned the evidence from Pallotti's tests that Vitamin A deficiency permits skin cancer. Vitamin A guards against Vitamin D injury. Some cancer-inducing substances have Vitamin D properties, also, which are linked with their unsaturated nature.

VITAMIN E

The conflicting reports on animal experimentation with Vitamin E, in cancer, bring sharply to our attention the fact that concentrated vitamins may not be beneficial in some diseases. Similarly, the sex hormones, which prove to be cancer inducing, are not to be used with safety. Yet these preparations can be purchased by anyone.

Wheat germ, one of the most potent sources of Vitamin E, has more than 75% of highly unsaturated fatty acids. It is therefore valuable in restoring the equilibrium of animals (and women) in which, with low Vitamin E, excessively active glands cause sterility. Re-absorption of embryos occurs just as in animals fed large doses of iodine. Wheat germ has been used by physicians to prevent abortion and to induce fertility. The experimental studies of Barrie of London in 1937 demonstrated how mother rats on a diet low in Vitamin

E produced young that had definite signs of pathological changes in the thyroid and pituitary glands. Some of the young were sub-normal, resembling cretins.

In 1931, Juhasz-Schaffer proved that wheat germ oil, added to tissue cultures of chick embryo, would accelerate their growth as much as 150% in 5 days. This is in line with the evidence that unsaturated fatty acids, added to tumors, caused their more rapid growth. And the experimental findings of Twort and others indicate that unsaturated fatty acids when added to the (unsaturated) shale oil derivatives increased their activity in producing skin-tumors in animals.

As we have elsewhere shown (page 200) the explanation of certain effects by glandular extracts may be through chemicals in them. For example, certain sex hormone effects can be identified with either iodine, or with *unsaturated substances*, including cholesterol and fats of the ovaries, depending on the method of preparation. Synthetic sex hormones are unsaturated hydrocarbons, and are capable of causing cancers.

In the case of the earlier extracts from the anterior pituitary gland, we have a considerable body of evidence that shows how they induced greatly accelerated growth of experimental animals. Robertson, successful with a growth hormone from the anterior pituitary, which he called "tethelin," used it experimentally to induce much more rapid growth of inoculated rat tumors. Erdmann in 1918 learned that there was threefold acceleration in certain chick tumors, after tethelin had been injected. Robertson emphasized the action of the unsaturated fatty acids in tethelin; Drummond and Cannan identified it merely as a mixture of lipoids (fatlike substances); therefore it is not surprising to learn that Ewe (1919) was able to inactivate tethelin with reference to growth promotion by adding to it *iodine*.

Nakahara by injecting fatty acids caused an increase in the resistance of mice to implanted cancers. This could be through adequate stimulation (but not exhaustion) of the glandular mechanism which regulates iodine and calcium. For Helmer (1936) has similarly caused inhibition in growth of experimental cancers by extracts of pancreatic fatty acids, designated as "unsaturated." Injection of small amounts of unsaturated substances may be defensive by activating glands of internal secretion which control the liberation of the

carcinolytic elements. We know that hyperthyroidism follows on such injections, as does the feeding of unsaturated fatty acids. And hyperthyroidism causes as much as 300% increase in the blood iodine; and 250% increase in calcium excretion.

In 1935, Severi learned that an excess of Vitamin E increased the resistance of *female mice* to injected cancers; but that in males Vitamin E apparently favored the growth of non-malignant warts. Here we have a marked difference in the male reaction which is due in part to the fact that males normally have much less fat in their bodies than females. Females are cyclic in their release of iodine (at heat or in the human menstrual period).

In 1934, and subsequently, Davidson, experimenting with two different types of diet, learned that animals that had received ample Vitamin E were more resistant to tar carcinoma than others on a less rich diet. He was stimulated to this test by noting that in some of the mice that developed tar carcinoma there were signs resembling those from Vitamin E deficiency. "They were weak, their hair was rough, their weight subnormal, and they were sterile, through testicular degeneration in the males, and through death of the fetuses in pregnant females." He continued his tests, and in 1937 reported on tests with 600 mice, extending over a period of 6 years. A combination of vitamins in the food, including Vitamins A, D and E, proved best in protecting the animals against repeated painting with tar. With lowered vitamins in the food, Davidson noted that the tumor threshold was correspondingly lowered, and tar carcinoma developed earlier.

It may be significant to mention here the fact that in vitamin deficiency, whether it be any one of the fat-soluble vitamins, there is a remarkable development of thyroid overactivity. And in cancer, Sümegi in 1938 has shown how rats, tested with adrenalin, resemble human cases with overactive thyroid glands. The action of tar, applied regularly, is to exhaust the supply of essential elements, and hence hasten the effects which may also be due to vitamin deficiency.

Davidson has used high vitamin diets in human cases of cancer and noted some improvement. He also administered to certain hopeless cases a filtrate from the tissues of newly dropped mice. In one case he describes a woman of 82, who had developed *cataracts* of both

eyes before she became a victim of cancer. A high vitamin diet, and injections of the filtrate from mouse embryos, resulted in regression of the cancer of the breast, after 4 months. General improvement in bodily condition was also induced. Newspaper publicity on this report has caused considerable adverse criticism, as might be expected.

Cameron in 1937, using diets that differed in proteins, salts, and fatty acids, and closely followed those of Davidson, learned that the "good diets" with wheat germ, green leaves of lettuce, and fresh milk did not prevent the appearance of tar-induced cancer, but that the growths were considerably delayed in appearance. His experimental studies with mice that were in part supplied from Dr. Davidson's colony can not be said to indicate more than a delay in the time of cancer development. The animals on the protective diet were in general resistant to toxic agents and heat, and were on the average heavier than those on the "bad" diet.

We do not need to run tests with experimental animals to know that after long continued exposure to certain "unsaturated" mineral oils sturdy men may develop "shale-oil" or "mule-spinners" cancer. Of this we shall treat elsewhere. (See page 209.) Such shale-oil cancer is readily induced in experimental animals. And the oils may be treated so as to render them harmless, through either hydrogenation or *saturation*. The oils with the highest "iodine-numbers" are most toxic.

Let us return to the matter of Vitamin E and wheat germ oil, for recent experiments seem most significant chemically and physiologically.

Thus far evidence has been conflicting about the rôle of Vitamin E and even of fatty acids in general. But we have a parallel example in the case of sterility. For, women who are sterile because of overactive glands, and generally run down condition, may be restored to health by Vitamin E and the unsaturated fatty acids. On the other hand, McCarrison and Mellanby more than twenty-five years ago showed that goiter and rickets were produced by wheat germ, and even by oatmeal.

Our explanation of the fact that Vitamin E may benefit animals that have cancer is that it will aid in stabilizing the glands, overactive in the disease. The fact that wheat germ oil *MAY* cause cancer is

explained simply as the action of *unsaturated substances* on glands, which by demanding iodine and producing goiter will ultimately cause exhaustion of the mechanisms that regulate growth.

The most recently reported work that indicates danger from the use of wheat germ oil, and other easily obtained medicaments, without a doctor's advice, is that of Dr. L. G. Rowntree and his associates, at the Philadelphia Institute for Medical Research. In experiments extending over a number of years, and first reported in 1937, these investigators fed a crude wheat germ oil, made by ether extraction, to more than 100 rats. In every animal fed there developed from one to several cancers in the abdominal region. Grafts from these cancers were successfully transplanted to hundreds of rats and developed into cancers also.

This is the first instance recorded where a product of vegetable origin has been used to produce internal tumors. It has long been known that, externally applied, certain unsaturated fatty acids accelerated cancer growth and even induced cancer formation.

Dorrance of Philadelphia was able to repeat successfully the experiments of Rowntree, but others have published reports indicating negative findings. As in vitamin and glandular research, differences in chemicals, animal strains, and technique are often responsible for conflicting results in the same laboratory.

In a letter to the author (1940), Dr. Rowntree states that with certain changes in the preparation of the wheat germ oil, used in feeding tests, *fewer tumors* appeared in his animals. On the other hand "we have a very large preponderance of animals on *injections*, with abdominal masses." At another laboratory, in close communication with Dr. Rowntree, similar large numbers of animals that were *injected* with wheat germ oil developed typical sarcoma. This recalls the evidence of Juhasz-Schaffer on wheat germ oil and the accelerated growth of tissue cultures (page 93).

Exception has been taken to my statements regarding the work of Dr. Rowntree's group, in a letter just received after reading proof (September 29, 1944). The writer encloses a fine summary with 11 abstracts of negative findings.

From Dr. E. V. McCollum's laboratory has come the suggestion that the carcinogenic agent in wheat germ oil might have arisen

through the action of peroxides from ether used in preparation. But the authors (Day, Becker and McCollum, *Proc. Soc. Exptl. Biol. and Med.*, 40, 21 (1939)) state that this theory was proved false, in their careful experiments.

Evans of California (same journal, 41, 318 (1939)) suggests that the rats in his tests may be of a sturdier strain than Rowntree's.

Pending further experiments and reports from Colonel Rowntree's laboratory, which are necessarily interfered with by the activities of our Medical Director of Selective Service, we shall have to attribute differences in results to differences in animals, technique and in the chemistry of the wheat germ used.

This author refuses to accept the category of one of those who present material in biased fashion. For he believes that there is an explanation, and a very significant chemical one, for most discrepancies in the various reports on vitamins, minerals, glands, and even cancer. "We fail to confirm" is an easy way to avoid that "get together" spirit so lacking in research as well as among nations. We are *all* working for the common good.

The delicate balance in the body between unsaturated substances and iodine is well shown in the experiments of McCarrison, who produced goiter, and of Mellanby, who produced rickets, by feeding wheat germ oil. For in each case the use of cod liver oil, with an appreciable (and recognized) iodine content, corrected the fat-thyroid-iodine imbalance. We have pointed out elsewhere that the great losses of calcium in rickets are due to overactive thyroid function, and thus corrected by iodine-rich cod liver oil, where the fatty acids are guarded. (Chidester, Ashworth, Ashworth and Wiles, *Int. Clinics*, 1934.)

To feed wheat germ oil of a very highly unsaturated nature might cause experimental cancer through its action on the glands. To inject wheat germ oil, even if it were not quite so completely desaturated, would still be a sufficiently unbalancing factor in the tissues to absorb and over-rule the inhibiting elements, and actually to hasten growth.

Natural sources of Vitamin E include not only the unsaturated fatty acids but carry with them essential minerals and other vitamins.

Kinosita in 1937, using rice as a basal food, was able to produce

liver cancer in rats by feeding a dye, known as "butter-yellow." But when he used wheat bread instead of the rice, the liver cancers were definitely reduced in number. But Sugiura, in 1941, found that wheat germ oil did *not* protect. *Wheat bread retains its minerals.*

Vassiliadis (1940) found that wheat flour protected rats against another cancer-inducing chemical, called amino-toluene.

In another study, Sugiura and Rhoads report that ether extracts from rice bran and brewers yeast will prevent liver cancer in rats given the cancer-inducing "butter-yellow" which is a benzene compound.

Such results indicate the need for more accurate inquiry into the antagonism of fats and lipoids to introduced hydrocarbons which are potentially carcinogenic.

"Every man's work shall be manifest."

—NEW TESTAMENT

VITAMIN F, ESSENTIAL FATTY ACIDS, AND THE LECITHIN-CHOLESTEROL RATIO

We have just shown how highly unsaturated fatty acids of Vitamin E may be related to the development of cancer. But it is important to consider the fact that, as in the case of other substances which are injurious or even cancer forming, their power to stimulate glandular function renders them also of *great value* in cancer. Moreover, the need for fats and fatty substances of a highly unsaturated nature appears in many diseases that involve glandular derangement, and could induce precancerous conditions. Unsaturated fatty acids aid in restoring the glandular balance.

While linseed oil has been known as a most valuable medicament for about 26 centuries, it was not until Burr and associates discovered the importance of certain of its highly unsaturated fatty acids that it gained its rightful place.

The writer has, since 1930, published reports that indicate how the "essential highly unsaturated fatty acids" are involved in the fat-thyroid-iodine balance of McCarrison. We are considering *these* unsaturated fatty acids under the heading of Vitamin F, a term that is in common use.

The affinity that iodine has for certain fats on account of their unsaturated nature has a most important bearing on the behavior of iodine in the metabolism of the body. When unsaturated fats are eaten, they demand iodine, and cause profound stimulation of the glands of internal secretion, all of which are iodine-reservoirs.

In the catabolic process of the cell contents which precedes the anabolic, the iodine is released from glands and tissues to unite with unsaturated fatty acids and fats, thus facilitating its action. Fat-bound iodine is extremely valuable in preserving normality of the endocrine glands.

Desaturation of fats is one of the chief functions of the liver, and its result is that highly unsaturated fatty acids are sent to storage depots, to be used in emergencies. The bile-iodine is liberated into the small intestine, and plays an important part not only in digestion but in all bodily processes.

In regions where the iodine content of the water and foods is not sufficient, there may be a thyroid imbalance. For iodine obtained from natural foods in proper balance will preserve the normal activity of most bodily functions. And it has been shown by Winternitz and others that *iodine in combination with fats* is easily assimilated in the body. It is especially important that we consider the value of fat-bound iodine in the body and the preservation of the glandular balance by such combined fats and iodine as may be *least disturbing to the metabolic processes*. Ingested fat cannot be adequately digested or absorbed without *bile*. Fats must be emulsified before satisfactorily digested. Here bile is involved also. Bile is rich in iodine.

Natural fats are, in general, mixtures of various fatty acids. All seeds contain fats, and some of the "fatty seeds" have as much as 50% true fats.

Fat, in the form of *phospholipids* and cholesterol-esters,* is a constituent of most body cells.

The phospholipids contain free acid (from phosphoric acid), nitrogen, and several types of unsaturated and saturated fatty acids.

* Esters are compounds consisting of one or more alcohol radicals and one or more acid radicals united by oxygen, chemically analogous to a salt; usually fragrant and sometimes used in flavoring extracts, perfumery, etc. Many esters belong to the group known as *fats* and lipoids. Numerous esters of low molecular weight are present in the essential oils: esters of acetic, benzoic, cinnamonic.

Fats which are normally insoluble in water become emulsified in the presence of phospholipids. And pure phospholipids, insoluble in ether, become soluble when in combination with fats or other lipoids. Thus, pure fats are not easily obtained except from tissues that lack phospholipids.

Lecithin, a phospholipid with the ratio of nitrogen to phosphorus of 1:1, is found in most living tissues, and is readily secured from egg yolk, liver, brain tissue, and from plant seeds. The *lecithins* always contain unsaturated and saturated fatty acids. And the liver yields lecithin with 4 pairs of double bonds and a very high iodine number. Thus, it demands much iodine, chlorine and bromine.

It is believed that fats are converted to phospholipids and transported to the mammary gland, which utilizes them and converts them back to neutral fats before secretion of the milk.

When the fat content of the blood rises, the lecithin content is correspondingly increased, while the cholesterol rises slowly. With decreased fat content, the phospholipids of the blood decrease, and the cholesterol becomes lower. Bloor concludes that both lecithin and cholesterol are involved in fat transport, and that fat is carried to the tissues in the form of *lecithin*.

The lecithin to cholesterol ratio was found by Bullock and Cramer (1913) to be higher in rapidly growing tumors than in slowly growing ones.

Robin (1919) determined the high water content of human cancers of the liver, stomach, and pancreas which is favored by lecithin. In the *most malignant sarcomas* and fibromas, Yasuda and Bloor (1932) discovered a much higher percentage of phospholipids, cholesterol, and neutral fat than in the normal tissues in which they were growing.

If glands of internal secretion are functioning normally, and if the diet is adequate, there will be growth control, and cancers will not normally arise.

Occurring in nature along with *saturated* fatty acids, and able to add iodine to themselves and transport it through the body, the *unsaturated fatty acids* are of great value. Iodized fatty acids are slowly and evenly absorbed, giving off their iodine gradually, and, *without iodism*, will correct glandular derangement safely.

As we have shown, cod liver oil, with large amounts of highly unsaturated fatty acids, saturated fatty acids, lipoids including cholesterol, and essential elements of great importance to the body, is, when extracted properly, a source of iodine in adequate amounts to insure the proper fat-thyroid-iodine balance. The unsaturated fatty acids present are not likely then to cause the exhaustion of endocrine glands, but rather to aid in their stabilization.

With such stabilization of the glands of internal secretion, the body is insured significant amounts of calcium, iodine, and iron. The proper cholesterol-lecithin ratio and the normal lipolytic functions may be regained, for adequate iodine will cause cholesterol accumulations to break down.

Cholesterol, a lipid (fatlike) substance, related to the higher alcohols, is found in large amounts in the most malignant cancers. It normally accumulates in the brain, the ovaries, the adrenals, and in other glands of internal secretion. A heavy fat diet of eggs and milk, bringing cholesterol, will cause arteriosclerosis in young children. This fact was discovered when such diets were given to young diabetics. Cholesterol constitutes a large proportion of the constituents of cataracts, gallstones, arterioscleroses and cancers.

Cholesterol chemically resembles the sex hormones, Vitamin D, the bile acids, and the powerfully carcinogenic hydrocarbon, *methylcholanthrene*, which is derived from a bile acid.

Removal of the thyroid gland is followed by greatly increased cholesterol deposits in the body. The simultaneous administration of cholesterol, with iodine, does not result in experimental arteriosclerosis, if the *thyroid glands* of the animals are functional. But cholesterol feeding without iodine will cause such arteriosclerosis. Ungar (1934) found that heavy doses of *di-iodyl* protected animals against sclerosis of the arteries, if given in large enough amounts even after thyroid removal.

In the skin, sun exposure and ultra-violet light irradiation will act on the cholesterol, and hasten development of skin cancers, as shown by Roffo of Buenos Aires. Iodine is activated and released from tissues by sunlight; hence the prolonged effect of the sunlight is to alter the chemistry of the skin, and when iodine has escaped from the lipoids and fats, the altered condition will permit unguarded cells to

grow excessively and form a cancer. Heavy sunning causes severe thyroid disturbances, and thus lowers resistance.

When the glands of internal secretion are exhausted and inadequate iodine is present, there may be great increase in cholesterol accumulations. And cholesterol has an inhibitory effect on the lipolytic enzymes (Mathews). There is in cancer patients a disturbed fat metabolism and an inability to split fatty acids of higher molecular weight (page 54).

In growing cancers we find substantial amounts of cholesterol, amino-acids, fatty acids (saturated and unsaturated), neutral fats, and minerals. The most rapidly growing cancers have high sodium and potassium, and low calcium and magnesium content. Both calcium and iodine are very high in slowly growing or in regressing tumors.

Iodine, extremely important in the distribution of these substances in the body fluids, is essential to facilitate oxidations, and to prevent precancerous accumulations of the growth-acids, hydrocarbons and lipoids.

The acceleration of growth in tissue cultures by unsaturated fatty acids, and even the evidence that in some cases of experimental cancer they may cause tumors to grow more rapidly, merely indicate the delicacy of balance between growth substances, as regulated by the glandular condition and the local growth center. For the unsaturated fatty acids that are capable of arousing the endocrine reservoirs to renewed activity, and thus *causing cancer regressions*, are also, when *locally applied* to a cancer, chemically able to unite with iodine, and temporarily to prevent it from causing the rapid breakdown of the growths which abundant iodine will do.

Results from tests with natural fats have been most conflicting. We may attribute variations to differences in the vitamins and minerals in the fats used, and also to the individual growth-chemistry of types of cancers studied.

Certain investigators have found that butter stepped up the growth of tar cancers in mice (Watson) and in rabbits (Oike). Others, using 40% butter, caused slowing in growth of *rat carcinomas*, but there was no influence on *rat sarcomas* (Benedict and Sugiura).

Baumann and associates have shown (1939-) that high fat diets may increase the rate of formation of some induced tumors, but that other types are not apparently influenced.

Miller and associates (*Cancer Res.*, 1944, 4, 153) showed that dietary coconut oil inhibited the origin of *induced* liver tumors in rats. The superiority of cod liver oil to coconut oil in slowing the growth rate of rat carcino-sarcoma 256 has been attributed by Haven (1936) to the fatty acids with longer side chains in the cod liver oil.

While we cannot rely too much upon the evidence from *induced tumors*, studies on spontaneous and on induced *leukemia* by Lawrason and Kirschbaum may be suggestive. Tests with diets high (32%) and low (3%) in fats were made (1) with mice of the high leukemia strain F, and also with (2) mice of the strain DbA that were treated with the carcinogenic substance *methylcholanthrene*. (Lawrason and Kirschbaum, *Proc. Soc. Exp. Biol. and Med.*, 56, 1, May 1944.)

The more rapid growth of mice on high-fat diet was accompanied in the high leukemia F strain (1) by slightly *earlier onset of spontaneous leukemia* than in their litter mates on low-fat diets. Our belief is that the high-fat diet increased the weight of the group and set up glandular disturbances that permitted leukemia to develop earlier.

In the experimentally induced leukemia (2) *later* appearance of the disease came in mice fed 32% fat. The authors suggest that oils of the fur could retard absorption of the methylcholanthrene by fattened mice.

There is considerable evidence that, in proper doses, the highly unsaturated fatty acids may induce such a mobilization of iodine as to cause cancers to break down. For such fatty substances demand iodine from the glands, fluids and tissues of the body. Glandular hyperfunction is induced and dispersal of growth substances is facilitated by the release of liquefying elements attacking tumors.

Nakahara injected unsaturated fatty acids and was able to cause increased resistance to the transplantation of spontaneous cancer in mice. Similar results were obtained by Helmer (1937) in chick sarcoma.

By feeding oleic acid, Freund (1932) set up conditions unfavorable to successful inoculations with carcinoma, and was able to inhibit the growth rate of carcinomas in animals.

Wheat germ oil (Davidson), butter fat (Caspari) and olive oil have been reported to be valuable inhibitors of tumor growth in animals. All these substances contain highly unsaturated fatty acids.

In their continued studies of the "essential unsaturated fatty acids" on recoveries from *skin lesions* that characterized the early discoveries, Burr, Evans, Brown, Cox and others learned that complex oils were better than the single fatty acids. It was also found that Vitamin F from *natural fat mixtures* were superior to any artificial mixtures. (Cf. Perlenfein, Report No. 3, Lee Foundation for Nutritional Research, Feb. 1942.)

Penn, in the belief that the carcinogenic properties of cholesterol or its decomposition products might be neutralized by their chemical and physiological antagonists, the *phospholipins*, has prepared lecithin extracts from various beef organs, and tested them with 9 patients suffering from cancer of the heart, breast, lungs, uterus, and abdomen. His report indicated improvement in 6 cases, three of them cancer of the breast. The lead is suggestive, in inoperable cases. (Penn, H. S., "Inoperable malignancy," *Med. Record*, 1935, vol. 142, no. 5, pp. 213-217.)

It will be remembered that Hansen (1933) was able to raise the serum iodine in babies with linseed oil (rich in unsaturated fatty acids). Moreover, Hart and Cooper (Report, Lee Foundation for Nutritional Research, Nov. 1941) were able to raise the serum iodine in cases of prostatic hypertrophy 300% by administering 5-grain tablets of the unsaturated fatty acids, linolenic, linoleic, and arachidonic acid. The rapid reduction in size of the prostate under such treatment is in line with the well-known effective action of *iodine* in prostatitis. Highly unsaturated fatty acids (termed Vitamin F) cause the liberation of large amounts of iodine from bodily storehouses. The thyroid gland shares with all the other endocrines its ability to liberate iodine and to mobilize calcium.

Haven found (1935) that to feed cocoanut oil favors the growth of tar carcinoma in rats. Such tumor growth was not stimulated by menhaden oil or cod liver oil. We attribute the lack of acceleration in the case of these oils from marine fishes to the fact that they have, in combination with sterols and fatty acids, large amounts of *iodine*, and can thus rapidly restore glandular balance. The stabilization of the endocrines will result in conservation of calcium and of the iron and iodine which facilitate oxidations, and aid in restoring the cholesterol-lecithin balance. Iodine disperses cholesterol, and is

markedly lipolytic, and is known to inactivate the growth substances of tumors.

The iodine numbers of the phospholipids of rat tumors were lower than muscle, according to Haven. This is in line with the discovery of Currie (1922) who found that the tissue fats near cancers had a very *high iodine number*, indicating that the tumors had seized iodine from adjacent cells, and robbed the incoming blood and the tissues of iodine in body fluids as they grew. The absorption of iodine by tumors is favorable to their growth, up to a certain point. Holler (1925) learned that cancer tissue was richest in iodine at the time that the tumors were breaking down.

Unsaturated fatty acids may, if fed exclusively in the absence of adequate balancing iodine, cause overactivity and finally exhaustion of the glands of internal secretion.

On the other hand, the administration of either iodine alone or of the highly unsaturated fatty acids is able to set up conditions that favor the mobilization of iodine, which can attack cancerous growths. The necessity for subsequent administration of unsaturated and saturated fatty acids, together with proteins, and carbohydrates, is self evident. And we must also furnish adequate iodine, iron, calcium, magnesium, potassium and phosphorus. Endocrine activity causes enormous losses of these substances and of the vitamins that are associated with their use and with proper glandular function. All the vitamins which have proved necessary for the restoration of the balance between proteins, carbohydrates, fats, and lipoids on the one hand, and minerals on the other, must be furnished in proper amounts.

VITAMIN H, AVIDIN, AND CANCER

Vitamin H is the term given originally by P. Gyorgy to the protective substance that prevented "egg-white injury." When fresh or commercial egg-white is fed to animals that lack Vitamin H, severe and fatal inflammation of the skin appears. This inflammation resembles the type seen in erysipelas.

The identification of Vitamin H with "biotin," an extremely potent growth substance, and the action of its *inhibitor*, obtained from egg-white, and now called "avidin," have raised the question of biotin-avidin balance in relation to cancer.

Too much *biotin* results in excessively rapid growth; and too much *avidin* causes the inactivation and non-absorption of biotin. Moreover, the fact that egg-white or its purified fraction "avidin" will cause skin conditions similar to those seen in erysipelas recalls the fact that so-called "spontaneous" regressions of cancers have been reported after fevers, including a number of cases of erysipelas. (See page 41.)

Biotin is found in bacteria, in yeasts, and in the tissues of higher animals as well. As little as 1 part in 400,000,000,000 parts of the culture medium will stimulate yeast cells to growth. Neither the iodine content of avidin nor the degree of *unsaturation* of biotin has been considered in relation to their action.

Drs. West and Woglom of Columbia University have studied the *biotin* content of cancerous tissues and of embryos. Domestic *rabbit embryo skin* contained 531 parts (microgamma) of biotin per gram as compared with 14 parts in the skin of the mother. *Tumors* of the skin in rabbits contained about 4 times as much biotin as normal skin tissue. (Embryonic skin and growing tumors are both rich in iodine.) Human lung cancers contained more than 3 times as much biotin as normal lung tissue. West and Woglom conclude (*Science*, May 30, 1941) that the presence of *biotin* in embryonic and cancerous tissues in amounts that are several times as large as in normal adult tissues indicates a difference in metabolism that is shared by tumors and embryos. They do *not* find it common to all tissues in which cells are rapidly dividing.

Biotin is linked with the growth-substances in embryonic as well as in cancerous tissues. It is not clear just how malignant teratoid cancers arise in the fetus, while it is still in utero, but some abnormalities in mammalian embryos, as well as in fish (used experimentally), are known to be due to nutritional and chemical insufficiencies or excesses as the embryos develop.

Avidin, prolonged feeding of which causes severe inflammation of the skin in various species of animals, and which combines with biotin and nullifies its growth-properties, would naturally seem to be suitable for tests in cancer. And we are indebted to a Science reporter for the *New York Times*, W. L. Laurence, for his stimulation of clinical trials of raw egg-white, from which "avidin" derives.

At the December (1942) session of the Radiological Society of North America, Dr. Ira Kaplan and associates reported that they had fed *three* cancer patients large amounts (three dozen) of raw egg-whites each day. Two of the cases were given supplemental X-ray treatment, and *all* the cases showed definite improvement in health with some cancer regression.

Here again, we apparently have an instance of a fever-producing and gland-activating agent which may be important as a dietary adjunct in the treatment of cancer. (See Fevers, page 41.)

The theory that large amounts of *avidin* will inactivate *biotin* and cause *cancers* to regress, or even will prevent their formation is, however, *not* supported by a case of egg-white disease reported by Dr. R. H. Williams, of Boston, in the *N. E. Journal of Medicine* (1943).

The patient had for some 40 years been eating raw eggs, together with wine. He consumed as many as 6 dozen raw eggs thus in a week, and finally came to the clinic with an eczema-like red rash. He was also afflicted with cancer, heart disease, urinary tract infection, and chronic bronchitis.

The hospital diet cleared up his rash, but the cancer growth was not affected. When he was placed again on his egg-wine diet, the red rash reappeared, but the cancer continued to grow. Suggestion has been made that the bacteria of the urinary tract infection were making *biotin* in sufficient amounts to offset the nullifying rôle of *avidin* on its growth-properties, and even to feed the growing cancer.

As stated, the inflammatory condition seen in erysipelas, and other diseases that produce fevers, is responsible for cases of "spontaneous" cures of cancer.

There is marked overactivity of the endocrine glands, particularly the thyroid and the adrenals, when the body combats bacteria. And, as we have pointed out, accumulations of the sterols, or of foods that demand *iodine* which they are prepared to absorb, will also set up hyperactivity of the glands of internal secretion. Tubercular patients with marked thyroid overactivity are thus unlikely to develop cancer, but to die of the tuberculosis before glandular exhaustion permits growth-acids and sterols to accumulate.

In the case described by Williams, it is quite possible that the effects of the wine-egg diet on the endocrines had rendered them in-

capable of coping with the bacteria, or the new growth. In considering the biotin-avidin balance, we should have data on the degree of stimulation exerted on the endocrine storehouses of iodine by the avidin; and the iodine numbers of avidin and biotin. There should be significance also in the actual *content of iodine* in the biotin. For proportionately small amounts of iodine will stimulate growth of cancers, and records are instructive with regard to the occurrence of *iodine* in growing cancers and in embryonic skin.

We have discussed the fact that cancers and embryonic skin are known to yield substances that prove effective in inhibiting cancer-growth in experimental animals, and we have identified this carcinolytic (cancer-destroying) action with their iodine content. (See page 140.)

As described in the previous section, the Memorial Hospital group headed by Rhoads had learned that if a diet containing "butter-yellow," which is ordinarily cancer-inducing, were supplemented by casein, cholin, cysteine, and vitamins of the B group, liver cancer rarely appeared in their experimental rats.

In further tests, Du Vigneaux and Rhoads, with their associates, added biotin to the protective diet, and the rats then developed liver cancer from the butter-yellow. Some factor in the biotin was responsible for negating the value of the protective diet.

Further studies, reported in August, 1943, at the Memorial Hospital, indicate that the butter-yellow itself is not cancer-inducing. But when the liver action on butter-yellow caused the separation of various chemicals, two of them were able to prevent the proper action of a liver enzyme. Without this enzymatic effect some of the liver cells became cancerous, while others merely died.

Pollack, Taylor and R. J. Williams (1942) cast some doubt on the conclusions of West and Woglum by showing that biotin was absent in human cancers and extremely low in rat cancers.

Later studies of West and Woglum (1942) indicated that tumor growth was independent of biotin and that avidin-treated animals were receptive hosts to cancer transplants which grew in the absence of biotin.

The search for chemicals that will attack malignancies, without injuring healthy cells, continues. We are not certain about the hazards of irradiating some of the carcinolytic elements. (See pages 112-139.)

CHAPTER VII

Cholesterol

Sterols, which are lipid (fat-like) substances related to the higher alcohols, are extremely important biologically. They are distributed quite generally among plant and animal tissues.

Sterols are sources of the "sex hormones"; they act as Vitamin D, in the cure or prevention of rickets, if still unsaturated; but if ergosterol or cholesterol is *brominated*, the antirachitic effect is lost. We attribute this to the "saturation" of the sterols which would otherwise induce overactivity of endocrines controlling calcium. Sterols accumulate in the organs in disease-inducing amounts, when old age has caused glandular insufficiency.

Cholesterol, found in the walls of arteriosclerotic blood vessels, and in lens cataracts, constitutes a very large percentage of the most malignant cancers. It was first obtained, in 1775, from gallstones, of which it is the chief constituent.

Cholesterol normally occurs in the blood, and is found in bile, milk, and the organs and tissues of the body. It is especially important in the glands of internal secretion, including the adrenals and ovaries. It is not found to any extent in muscles, but is proportionately high in the brain and the lungs. In the bile, about 4% of the excreted solids consist of cholesterol; in the skin, it is excreted by way of the sebaceous glands.

Cholesterol has been shown to be closely associated with the development of skin cancer by Roffo. At the Cancer Institute of Buenos Aires, Roffo learned that skin cancers developed chiefly in those regions that had been exposed to the sun. With 61% of the face cancers in the nose region, Roffo correlated the occurrence of 50% more cholesterol in that region than in the cheeks, where he found only 18% cancerous. He experimented with rats exposed to sunlight, and to ultra-violet rays, and was able thus to induce skin cancers. (See page 92.)

Dr. S. Peller reported at the Atlantic City meeting of the American Public Health Association, October, 1941, that skin cancer which kills only 5% of its victims apparently *protects* or immunizes against internal cancers, known to be about 90% fatal. Peller suggests that ultra-violet light might be used to induce artificial skin cancers, and thus to "vaccinate" against other and mortal cancers. Peller is only hopeful that such procedure would protect about 50% of the cases treated.

An opposite view of skin cancer is held by Dr. Shields Warren of Boston, who studied 1149 patients with skin cancer and found that they were markedly susceptible to second attacks of cancer elsewhere in the body. We believe that systemic effects would here involve the exhaustion of protective endocrines, which permit cancer.

Since clinicians have been using a high-fat diet in the treatment of diabetes, an unfortunate development of arteriosclerosis in children has appeared. Children receiving excessive amounts of eggs and milk, which are rich sources of cholesterol, proved to have premature scleroses of the blood vessels. It has long been known that experimentally arteriosclerosis is induced in rabbits by cholesterol feeding. Here, investigators have also shown that simultaneous administration of thyroid extract, or iodine, prevented such arteriosclerosis.

Gallstones, which are more than 90% cholesterol, develop in rats on a diet lacking Vitamin A. As we have pointed out, such a diet induces profound disturbance and ultimate exhaustion of the thyroid gland.

Cod liver oil, containing adequate iodine, prevents the development of gallstones in the control animals that receive such a deficient diet. And Tsuki was able to show by X-ray photographs that cod liver oil would cause the excretion of gallstones that had accumulated in rats on the Vitamin A-deficient diet. The medical profession have been slow to realize the chemistry of such action, and some still use olive oil, which is not of any great value except to stimulate the gall-bladder.

Schmid, in 1937, experimented with the gall-bladders of pigeons, placing in them a solution of irradiated ergosterol in linseed oil. After 1 year, he found that epithelial tumors had developed in the walls of the gall-bladder.

Analyses of cholesterol in cancers have been made by a number of investigators. In 1919, Dewey found that the chief lipid in jaw tumors was cholesterol; Iwano in 1924 corroborated the discovery of Bennett in 1914 that the cholesterol content of cancer tissue increases with the age of the tumor, and showed that the cholesterol content was highest in the central portion of the growth.

In 1932, Yasuda and Bloor learned that the most malignant sarcomas and fibromyomas contained much higher percentage of cholesterol and the phospholipids than in the tissues where they were growing. They also found such high cholesterol in adenomatous cancer of the thyroid gland.

Currie, in the same year, learned that in cancer patients the cholesterol accumulations in depot fats were greatly increased. This suggests faulty handling of cholesterol by a body invaded by cancer. This again may be correlated with glandular imbalance. Identification of *high* blood cholesterol with the breaking down of cancers has been attempted by other workers. And Rowntree of London describes the reduced amount of blood cholesterol in advanced cancer cases. We may very well link this with inactivity of the protective glands. For *cholesterol* in the blood is *reduced* with thyroid exhaustion, and is *increased* when it is active.

In 1913, Robertson was able experimentally to accelerate the growth of rat carcinoma by direct injections of cholesterol into the cancers.

Corson-White supplied cholesterol in excess, and noted rapid tumor growth in animals (1919). In 1924, Borst reported similarly for spontaneous and implanted cancers in rodents.

It has long been known that operative removal of the thyroid permits accumulations of cholesterol. Moreover, Duncan of England, and Hoskins of the U. S., have been able to cure some cases of insanity involving excessive cholesterol accumulations in the brain by using thyroid extract.

CHAPTER VIII

Minerals

"How Nature universally delights in a quiet stability; all things thrive and flourish by communicating, reciprocal aid."

—I. BARROW

The fact that numerous clinicians advocate a plentiful supply of fresh fruits and vegetables, in treating a variety of diseases, is an indication that they believe in minerals, naturally balanced.

Horace Packard, in the *Boston Medical and Surgical Journal* for 1912, said, "People who inhabit the tropics where a bountiful food supply of fruits and vegetables rich in *food-salts* is consumed without cooking, are cancer-free, or afflicted slightly."

F. T. Marwood of England, who is an adherent of the salt theory of cancer, has directed attention to the fact that "in their raw state, fruit, vegetables, and cereals provide all the necessary food-salts that we need for our well being and preservation." There must be a grave risk in consuming salt so immoderately as we do today.

Rumley has said, "Aside from over-eating, another factor needs to be considered, viz., the change in character of the food we eat. Due to food processing, we no longer eat *whole foods*. Sugar is but one of the constituents of the sugar beet and the sugar cane, and yet sugar is 99½% pure carbohydrate of a single form. The *minerals, salts, proteins*, and other natural elements of the plants are removed and thrown away. We eat sugar to the extent of 104 lbs. per capita each year."

Our ancestors ate natural, balanced salts, and unprocessed food-stuffs with the carbohydrates and fats and proteins rich in protective elements. This natural type of foods has been until recently characteristic of savage races. Doctor Weston A. Price, of Cleveland, has studied the present diets, and carefully investigated the type of diets used by primitive people before civilization caused them to alter their food habits.

He cites the statements of Dr. J. Romig, of Anchorage, Alaska, on his experience of 36 years with Eskimos and Indians. Dr. Romig stated that he had never seen (in 36 years) a case of malignant disease among the truly primitive Eskimos and Indians, although it frequently occurs when they become modernized. "The acute surgical problems requiring operation on internal organs, such as gall-bladder, kidney, stomach, and appendix, do not occur among the primitive, but are very common problems among the modernized Eskimos and Indians." (W. A. Price, "Nutrition and Physical Degeneration." P. M. Hoeber, Inc., 1938.)

As a result of this experience, he now sends patients with tuberculosis and other diseases back to primitive diet and primitive living conditions.

As we have shown in a number of articles in medical journals, women between the ages of 15 and 45 are more susceptible to tuberculosis because of cyclic losses of iodine, iron, and calcium, which the body needs.

The mineral salts are necessary to maintain normal physiological equilibrium and to control body processes. If mineral salts are withheld from the body, death ensues much more rapidly than from the withholding of proteins, carbohydrates or fats. The salts of the body in solution provide the proper medium for living tissues; and in organic combinations they furnish the elements for the formation of tissues themselves.

As in all forms of growth, there are certain elements which are directly concerned with the speed in growth of cancers and in their prevention. Since these elements are regulated in amount and in distribution by the diet, but also by the proper functioning of glands, it is appropriate to consider them at this time.

CALCIUM

Calcium, termed by many physiologists the most important element, is the one found in largest amounts in animals. Calcium salts are necessary in the coagulation of blood and milk; and for the formation of bone. The normal beating of the heart is dependent on the relationship between sodium and potassium salts, with calcium. Cal-

cium aids in preserving the alkalinity of the blood and is thus necessary for the preservation of teeth and bones.

Calcium assimilation depends in part on the protein intake. It plays an important part in the assimilation of fats. Normally, calcium combines in the liver with neutral fats to form soluble lipoids (fat-like substances) which are readily taken up by the blood.

All of the glands of internal secretion are iodine reservoirs (page 140), and it is known that their increased activity is followed by greater losses in body calcium. Our explanation of this fact is that the released iodine will cause fats to be separated from calcium combination, and that it then circulates through the body along with cholesterol, fat-droplets, and sugars. Since calcium and iron are bound together in the bony storehouses, we find that anemias appear after the increased activity of the thyroid gland which comes in women periodically, but markedly at puberty (chlorotic anemia), and at the menopause. Thyroid extract and liver extract stabilize the endocrines, benefitting anemics.

Even under normal conditions of living, the body requires about 0.75 gram of calcium in an adult each day; and a child needs about 0.33 gram, according to estimates. From 60% to 90% of the calcium is eliminated through the intestine, in the feces, and from 40% down to 10% in the urine.

Between the ages of 15 and 45, women lose at the menstrual period cyclically, during 2 or 3 days of each month, considerable calcium. Calcium requirements of nursing and pregnant women are three times the normal adult requirements. During puberty and at the menopause, glandular overactivity causes excessive losses of calcium, iron and other elements. Similarly, men, under a severe mental strain, or those engaged in heavy physical labor, require more calcium to replace losses.

The glands of internal secretion are all concerned with the proper distribution and utilization of calcium. When the thyroid gland is overactive, experimental animals are known to lose 250% more than the normal amounts of calcium.

Rickets, a deficiency disease, has been for some time associated with a lack of "Vitamin D," and has been treated successfully, by cod liver oil. The discovery that irradiation of certain lipoids, in-

cluding ergosterol and cholesterol, conferred on them the quality of benefitting rickets, has led to excessive sun exposure, and even to excessive use of the synthetic products. In fact, too much Vitamin D is extremely injurious. Here we find that the exclusive use of calcium is not beneficial. That cod liver oil is superior to synthetic sources of Vitamin D has been admitted, but the writer and associates have first furnished evidence as to *why* this is so. (*Int. Clinics*, 1934.)

In experiments with "antuitrin S," an extract from pregnancy urine, we attempted (1934) to induce the simultaneous maturing of several eggs, at an early stage in the development of chicks, by injections into their wing veins of small amounts of the extract. We secured rickets. Careful study of conditions disclosed the fact that we had induced preliminary overactivity of the thyroid gland. Others had reported *thyroid disturbance*, but had not carried their experiments with pituitary extracts or extracts from pregnancy urine beyond the initial associated stimulus to sexual prematurity, or in some cases to the following thyroid derangement. The students of sexual maturity, and of simultaneous ovulation of many eggs, have failed to realize the definitely contributory action of iodine. It is unfortunate that synthetic "sex hormones," known to be cancer-inducing, are in use when the *complete ovary* furnishes a safer, iodine-rich extract.

In our report (*Int. Clinics*, 1934) we showed how excessive amounts of the unsaturated fatty acids, on the one hand, or of thyroid extract, or iodine, or even the rays of the sun, which activate iodine, would cause thyroid overactivity, and result in rickets. True rickets has been found to be associated with hyperactive thyroid glands in Murray's studies. He also identified it in puppies on a diet rich in calcium. This is readily understood when we remember that Hellwig has caused *goiter* in rats with an excess of *calcium*. And *iodine* benefits animals that have developed rickets after excessive intake of unsaturated fats.

The reason for discussing rickets so fully is to identify overactivity of the thyroid gland with excessive calcium losses. It will be noted that we have also presented evidence that excessive sun exposure and excessive amounts of unsaturated fatty acids may also cause thyroid hyperfunction. The fat-thyroid-iodine balance of Mc-

Carrison (page 65) is essential and is easily disturbed. This is an explanation of why Vitamin E may serve in some cases as a beneficial agent, in offsetting with its fats and excess of iodine; but in others as a means of overactivating, and exhausting the protective glands. Such a condition could result in cancer, in Rowntree's tests, with ether-extracted wheat germ oil, just as it would in soot; and wholly desaturated substances can rob the skin of protective iodine, or can, when eaten, cause unusual overactivity of glands, to be followed by their exhaustion.

The classic interpretation of Vitamin E is that it cures sterility. As a matter of fact, the Vitamin E-deficient diet given to experimental animals is one that *contains no fats*, and that does have a *salt mixture* which induces goiter. The addition of unsaturated fatty acids aids in normalizing the glands, and fertility results.

A common report on avitaminosis E effects is that young animals are reabsorbed and cannot develop. Unguarded *iodine* causes this. In 1918, the writer attempted (at the Wistar Institute) to induce sub-normal development of embryos in pregnant rats by giving the mothers heavy doses of thyroid extract. Autopsies disclosed the fact that the animals, iodized after they had become pregnant, were *reabsorbing* their embryos. Since thyroid and iodine administration causes the liberation into the blood and body fluids of iodine and calcium, it is possible to identify this process of destruction of embryos, with the breakdown in cancers secured by glandular therapy.

It is also possible to correlate the *successful treatment of cancer* by radiations with this chemical action. For we know that iodine is activated by radiant energy; and that limited radiation will increase the storage of calcium and phosphorus. (See page 144.)

Calcium and Cancer

With statistical data at hand which suggested that certain limestone regions furnished records of extremely low cancer mortality, investigators found that the serum calcium of cancer patients was much lower than in normal persons. In 1924, Reding, comparing the blood of cancer-free families and cancerous ones, learned that the blood serum of cancer-free families was higher than in the relatives of cancer patients.

In 1905, Clowes and associates reported that in 100 mouse-tumors the rapidly growing ones contained a higher percentage of potassium and a very small amount of calcium. The older, slowly growing cancers in the process of *necrosis* had less potassium and *high calcium*. They also showed that cancerous tissues have an increased permeability (penetrability) to water-soluble substances. As a matter of fact, rapidly growing cancers, like all tissues that grow rapidly, have an excess of water, and an excess of liquefying potassium. The presence of a jellifier, calcium, is associated with reduced water content, and naturally a lesser tendency to spread, by growth or by splitting up and scattering as metastases.

Willy Meyer, in his book "Cancer," in 1931 had developed the idea that alkalosis, in which calcium is low, is induced by abnormal functioning of the sympathetic nervous system. Excessive potassium and lowered calcium favor the rapid growth of cancers, he shows. On the other hand, a condition of acidosis, with adequate calcium, induces a dehydration of the cells, and slows growth. Meyer was early impressed by the evidence of Busch and others that erysipelas and other feverish conditions caused "miraculous cures" of cancer. He has identified *acidosis* with such fevers, and also with the beneficial effects of starvation, and of some sera, and of calcium administration—all reported to cure cancer. We shall discuss other factors in their proper time, but shall now consider calcium.

Rapidly growing tumors, like all other tissues of rapid growth, have an excess of water. They also have an excess of potassium, the *liquefier*, and a reduced amount of calcium, the *jellifier*, which dehydrates, and prevents speedy dispersal of tumor fragments. Clinicians with whom the writer has been in close touch for the past 10 years have used calcium as an adjunct to other cancer treatments with distinguished success. It is beneficial in many cases other than bone sarcoma, but its value in other types of cancer is not fully appreciated. In fact, one prominent radiologist informed me that he had up to that time limited its administration to those cases where the *bones* were involved.

McDonald and others have emphasized the fact that acidosis victims are practically immune from cancer. Guy, Ferguson, and their followers are convinced of the value of hydrochloric acid therapy in

cancer, as in a number of other diseases. Chlorides will make calcium available by causing endocrine activity. All the endocrine glands control calcium.

Katase, Paik and others have proved that calcium is effective in animal cancer. Shear, in 1933, cited literature that indicates the retarding effect of calcium on cancers.

In treating the well-known disease involving excessive losses of calcium, termed "osteomalacia" of pregnant women, Blair Bell was first to report successful surgical attack by removing the ovaries. Ovariectomy conserved calcium. In 1900, Boyd, familiar with the records of veterinarians showing how, after spaying female dogs, breast cancers had regressed in some, adopted the procedure of ovariectomy in human cases of mammary cancer. He used thyroid extract as a supplement to the surgery, and reported success. Other clinicians, down to the present day, continue to remove the ovaries in some cases of breast cancer, usually in women near the menopause.

Our first knowledge that removal of the ovaries of young mice would prevent development of breast cancers in strains where it was very common came from the report of Lathrop and Loeb in 1916. Loeb found that greatly reduced cancer incidence came if the ovariectomies were performed on animals under 6 months of age.

Cori, in 1927, demonstrated that in cancerous strains of mice ovariectomy, when the females were only from 15 to 28 days old, was able entirely to prevent mammary cancers from developing.

Murray, in 1928, having demonstrated that virgin females of cancerous strains were more resistant to mammary cancer development, used ovary transplants into castrated male mice, and caused cancer of their breasts.

More recently Lacassagne, of Paris, and others have used the female sex hormone, *folliculin*, and by regular injections have produced mammary cancer in male mice.

There is a close relationship between the thyroid gland, the sex glands, and the development of breast cancer in either sex. As early as 1848, cases of *goiter* in men followed by abnormal functioning of the breasts have appeared in the literature. In some cases, this goiter in males may be followed by breast cancer as well. We shall defer discussion of the types of cancer that involve glands which control

calcium, and iodine, until later. But the fact must now be emphasized that all glands of internal secretion *control calcium*; and that all of them *contain iodine*. (See pages 155 and 159.)

The use of *limited radiation* with X-rays and radium serves to increase the storage of calcium and phosphorus. And Stransky found that radioactive waters promoted the increased storage of calcium in rabbits. (See "Iodine in Salt Springs," page 134.) But heavy radiations cause excessive losses of calcium, and derange glands of internal secretion. Heavy radiations also increase the sugar, and thus hasten cancer growth by permitting a greater lactic acid accumulation.

We shall evaluate radiant energy elsewhere. (See page 144.)

PHOSPHORUS

Phosphorus is found in largest amounts in the organs that have the greatest vitality, and in tissues where growth-processes are most active. In the body, the proper balance between phosphorus and calcium must be retained, or rickets will result. In the bones, proper calcification is secured by the deposition of calcium-phosphate.

Combinations of phosphorus with proteins, termed phosphoproteins, which are secured from cows' milk and from eggs, will yield phosphoric acid when acted on by water. Phosphoric acid has been used to stimulate the thyroid gland in obesity by Koehler and others. Of course, hyperthyroidism will induce losses of phosphoric acid, also.

Phospholipids are fatlike combinations of lipoids, with nitrogen, and phosphoric acid. The best source of phospholipids is brain tissue. The writer has identified the nerve impulse with iodine-phosphorus combustion. Fats which are normally insoluble in water become emulsified in the presence of phospholipids. Fats must be converted into phospholipids before they can be utilized by the mammary glands. Conversion into neutral fats comes before actual secretion of milk occurs.

During lactation, large amounts of phosphorus are needed. This is true in all periods of growth, and in pregnancy as well. Similarly, in cancer, where calcium and phosphorus losses are heavy, it is necessary to furnish both in proper balance to prevent injury by either. White flour and fatty meats lack phosphorus. Marine foods, lean meats, and whole grain cereals supply it, along with the necessary

calcium and other minerals. For phosphorus is found in the body, closely associated with potassium, sodium, magnesium, and iron.

Riché, in 1931, described the use of magnesium and phosphoric acid in 2 cases of cancer of the liver and the stomach. He reported cures which had then lived 5 to 7 years respectively. At a conference in a New England hospital in 1938, this writer heard the report by a clinician of a case that he had seen in Florida the previous winter. The successful use of phosphoric acid in this undoubted case of cancer supported Riché's findings. And naturally in discussing the report the writer linked the effect with *thyroid stimulation* by phosphoric acid which was clinically demonstrated by Koehler.

Direct action of iodine and phosphorus would occur in cases of mammary cancer, relieved by a number of measures. (See page 229.) For diet, certain medication, even a proper mental attitude, will all insure the proper physiological function of the glands that control calcium and phosphorus in the blood. And these glands are iodine reservoirs.

The Radiation Laboratory of the University of California has been able to advance our knowledge of radioactive phosphorus. Erf, Tuttle and Scott have shown that in mice, glucose, cod liver oil and oleic acid (in the order named) have some influence on the absorption of radio-phosphorus into the body. (L. A. Erf, L. W. Tuttle, and K. G. Scott, *Proc. Soc. Exp. Biol. and Med.*, 45, 2, 652-657, November, 1940.)

At the same laboratory, Marshak reports greater uptake of radioactive phosphorus by tumor nuclei than by liver cells. Cell division is faster in the tumor cells. (A. Marshak, *Science*, vol. 92, No. 2394, pp. 460-461, November 15, 1940.)

Using radioactive phosphorus furnished by Dr. E. O. Lawrence from the Radiation Laboratory (Lawrence-Cooksey cyclotron), a group at the Memorial Hospital in New York have introduced radioactive phosphorus into the body fluids of patients about to be operated for cancer, and also in certain cases where death by cancer was imminent. The operated or autopsied cancers showed that the radio-phosphorus had settled in diseased tissues, and barely affected the normal cells. The burning power of the phosphorus was comparable to that of radium. The Memorial Hospital group (headed by Dr.

J. M. Kenney) are especially hopeful for important results in bone cancers.

There is a possibility that irradiated phosphorus may act with the iodine of cancers and cause rapid regressions. For, as we have shown, there is considerable evidence that iodine is selectively absorbed by cancer tissue; and, when irradiated, will cause rapid destruction of malignancies. (See pages 138-141.)

Justus records the fact that iodine is present in all nuclei. Sajous has emphasized the fact that iodine is most active where phosphorus is known to be most plentiful. Wilson says of iodine with phosphorus, "If a fragment of phosphorus, lying on a plate, is sprinkled with iodine, the substances unite, and heat enough is produced to kindle the phosphorus." (Cf. Justus, *Virchow's Archiv.*, 176, S. 1, 1904; Wilson, "Inorganic Chemistry," p. 284, 1897.)

It must be emphasized that an excess of phosphorus may cause an imbalance with calcium, and have serious results on the endocrines, which are already overtaxed in cancer. Simultaneous administration of calcium and of fats, as found in the best cod liver oil, and supportive use of Vitamins B and C, may tend to protect against untoward effects.

The use of irradiated iodine, without activating phosphorus directly, may bring into play the beneficial effects of several activated elements.

POTASSIUM

Potassium is necessary for the development of cells, especially those of the blood and of muscle. Miller showed (1918) that the growth of rats was greatly retarded by reducing the potassium below approximately 0.1%.

Potassium salts are indispensable in certain organic combinations. They aid in the formation of proteins, of fats, and of the carbohydrate glycogen—from glucose. The liver contains twice as much potassium as sodium. Potassium is found in red blood corpuscles, in milk, and in the brain in considerable amounts. Animals deprived of potassium show much retarded muscular development. Potassium salts are found chiefly in vegetable foods. In fact, scurvy in adult animals has

been linked by some investigators with the absence of potassium, since fresh vegetables supply so much of it.

An excess of potassium causes increased excretion of sodium and chlorine in the urine. Potassium stimulates greater water secretion.

Potassium and Cancer

Beebe, in 1904, showed that human cancers of rapid growth are richer in potassium than those which are degenerating. Clowes, in 1905, reported that potassium was low in old, slowly growing tumors in mice, but that it was high in the rapidly growing ones.

As mentioned before, Willy Meyer has identified the condition of *alkalosis*, favoring cancer development, with deranged functioning of the sympathetic nervous system, which permits *potassium* influence to predominate over calcium influence.

Epstein, in 1932, examined 52 benign or malignant cancers for their potassium content, and found that the more malignant the cancers, the greater their content of potassium. Shear (1933) has presented a most valuable discussion of the rôle of potassium, sodium, magnesium and calcium in cancer, and concludes that potassium may have a slight stimulating effect, while calcium slightly retards cancer growth. (Shear, *M. J.*, 1933; *Am. J. Cancer*, 18, 924-1024.)

The Norwegian, Dr. F. G. Gade (*J. of Cancer Res.*, Oct., 1921), has shown how erroneous conclusions on the effect of personal contact may be drawn from cancerous families in which both husband and wife developed the disease. He inclines towards an explanation that involves *erroneous* or over-nutrition, and says, "Married people will as a rule live under identical conditions, and partake of the same food." Gade cites the work of Blumenthal with rats that had been inoculated with cancer. Blumenthal found that "the growth of inoculated cancer in rats was accelerated when the animals got a surplus of potassium in their food, but retarded by a surplus of calcium."

In opposition to the findings against potassium, we have distinguished authorities who present evidence that potassium salts are *beneficial* in cancer.

Forbes-Ross in a widely quoted book ("Cancer, the Problem of Its Genesis and Treatment," London, 1912) says, "Assimilable salts of potassium, when administered to a bona-fide case of cancer, will be

found to benefit the patient in an astonishing manner, and will never cause the least harm even to the most feeble sufferer."

The distinguished founder of the New York Skin and Cancer Hospital, Dr. L. Duncan Bulkley, who believed that "meat constitutes the precancerous diet," was a firm believer in the value of potassium. In his book, "End Results in the Medical Treatment of Cancer," 1928, reports on the treatment of 900 cases of cancer showed that 60% of them were cured by potassium administration. Previously, without such potassium supplement, the percentage of cures was only 10%. Dr. Bulkley prescribed an extract made by boiling down the water in which potatoes and other vegetables were cooked, to insure retention of the valuable *potassium*. It should be pointed out that other valuable minerals are thus conserved. In fact, Remington (1929) has studied the potato as an index of iodine distribution.

Kylin (*Med. Clin.*, 1925, 21, 1268) has shown that *potassium*, injected intravenously, diminishes the *blood sugar* and the blood pressure, thus acting like insulin. We have elsewhere shown how successful some clinicians have been with *insulin* in cancers (page 183).

It is possible that potassium, by its laxative effect, may aid in preventing rectal cancer. But here iodine is involved also.

Potassium nitrate, called "tekarkin," has been sold as a cancer remedy. Of its value, no unbiased reports have been available to this writer.

The *iodide of potassium* is an old remedy long used to "thin the blood." Van den Velden found that *potassium iodide* diffuses readily into cancer tissue. Bourignon was able to liberate iodine from potassium iodide by electrical ionization, and thus to break down scar tissue in human cases. The writer was once privileged to hear the late Dr. James Ewing advise a cancer surgeon to give *potassium iodide* in his post-operative treatment. Then, turning to me, he said, explosively, "You don't think that I have worked on cancer for more than 40 years without having some of the same ideas that you have, do you?"

High Potassium and Iodine in Relation to Regressing Breast Tumors

Dr. Helen Ingleby, in 1932, reported the rapid growth of mammary tumors in women from about the middle ten days of the cycle

up to a day or two before the onset of the menstrual period. Tumors either became evident for the first time or, if present, increased in size up to that time. Early in the menstrual period, the breast tumors *regressed rapidly*.

From our own work on experimental embryology, and cancer in mice, we have accumulated data furnishing an explanation of how changes in the blood chemistry are involved in the process described by Ingleby. For the elements *iodine* and *potassium* are involved in the onset of menstruation itself, and they are in highest concentration in the blood as menstruation begins.

In several medical journals, we have correlated Ingleby's findings with the reports of Maurer and of Curtis that there is a period of the greatest *iodine* concentration in the blood, just before menstruation begins. Spiegler has shown that *potassium*, at its lowest concentration in the blood at the end of the flow, progressively increases to its *maximum concentration*, just as the next menstrual period begins. (Spiegler, *Archiv. Gynäkol.*, 1930, 143, 248-.)

Under ordinary conditions, *potassium*, *iodine* and other liquefying elements transport to the breasts substances that do not accumulate there unless physical or chemical conditions favor such a "new growth." The great increase in potassium and iodine at the menstrual period does hasten the regression in size of the breasts, almost invariably then enlarged.

A single blow on the breast may, however, produce abnormal conditions in the mammary blood vessels or lymph ducts, while fear, worry, faulty nutrition, or the introduction of certain chemical stimuli may cause a deranged sex cycle and tumors may develop.

In experiments with rats Ingleby induced *cystic* condition in the breasts by first deranging the sex cycle. Geschickter (1939), after 23 days of treatment with the female sex hormone *oestrogen*, produced mammary cancers in rats. Metastases migrated to the adjacent lymph nodes, and to the lungs in several instances.

The glands of internal secretion, which normally aid in regulating the circulation of adequate amounts of essential minerals, may be deranged as a result of dietary insufficiency, or by an excessive amount of some types of food. Through the nervous system, worry and fear may cause profound hyperactivity of some of the glands, including the

pituitary and the thyroid gland. Such glandular overactivity causes the loss of large amounts of essential vitamins, including Vitamins A and D, along with necessary fats, proteins and carbohydrates; vast amounts of calcium, iron, potassium and iodine are excreted. Chemical imbalance is great. The normal processes of growth, removal of waste matter and potential sources of infection are thus interfered with. A *lump* may form.

With the deranged function of the vascular system and altered blood chemistry, there are possible accumulations of some of the most potent cancer formers, in the breasts. For in the blood passing through these highly vascular glands, we find lipoids, including cholesterol; various amino-acids, fatty acids, and products of the bile acids. One of the degradation products of bile acids, *methyl-cholanthrene*, studied by Dr. L. F. Fieser, is capable of inducing almost 100% of sarcomas within 4 months in susceptible strains of mice. Mammary cancer appears in mice when methyl-cholanthrene is applied to the skin of the back. Evidently the reaction is a systemic one.

In Ingleby's cases, the growth of breast tumors is made possible, we believe, by the fact that *small* amounts of potassium, iodine, and other liquefiers in the intermenstrual days transport in the blood to the breasts growth-substances including cholesterol, amino-acids, fatty acids, and the products of bile acids. The presence of *cysts* or other *lumps* favors the accumulation of "new growths" which continue to increase in size until the *potassium* and *iodine* have reached their *peak*, at the time of menstruation. Coincidental with the sloughing off of the lining of the uterus we find rapid disintegration of recently accreted portions of the breast tumors. Unfortunately these may migrate as metastases to the lungs, vertebrae, or elsewhere.

Increased thyroid activity is characteristic of the menstrual period, and since hyperthyroidism causes an increase up to 250% in *calcium*, some control of metastatic dispersal of the lumps will occur, unless the thyroid itself has been exhausted. For calcium dehydrates tumors, and aids in preventing the excessively rapid sloughing away that favors metastatic dispersal, or may prove fatal.

Dr. Ingleby's clinical studies show how it is possible for some women to have "lumps" in the breast that will disappear at the time

of menstruation. Many normal women have recorded lumps in the breast which remained only a short time, and then "spontaneously" went away. But such a delicate balance exists in the chemistry of the body fluids, and the protuberant breasts of women are so susceptible to injury, that it is dangerous to delay consulting a physician if any *lumps* appear.

Dr. G. S. Foster (1942) believes that all women should be educated to seek their doctors twice a year and have the breasts thoroughly examined. He says, "Breast malignancy holds forth a greater opportunity for eradication in the next two decades than any other type of malignancy in the human body." But he also deplors the fact that there are still too many doctors who, after locating a tumor in the breast, will advise to "wait a time and see what develops."

H. C. Taylor (*Surg., Gynecol., and Obstet.*, 1936, 62, 562-), in reporting on 261 cases of diffuse breast disease, found that in 82 cases the onset of breast and menstrual symptoms was practically simultaneous. In 11 cases, breast cancer followed the operative removal of the uterus. Irradiation of the *thyroid gland* caused improvement in two cases where the thyroid was involved, with the breasts.

SODIUM

Sodium predominates in the fluids of the body, including the blood serum; inside the cells potassium is found. Sodium is the chief base of lymph and serum, and it facilitates the absorption of protein foods and increases tissue metabolism. Sodium is associated with excessive amounts of water.

Sodium carbonate is essential to the transportation by the blood of carbon dioxide from the tissues to the lungs. Sodium chloride is demanded chiefly by vegetarians, and animals like the deer will travel long distances to "salt-licks." Carnivorous animals, and savages who live on meats, do not require salt.

Sodium is required in amounts of only about 5 grams a day by humans; but, with their degenerated taste buds, persons who season their foods may consume from 10 to 20 grams of salt per day and suffer thereby.

Sodium chloride has been used experimentally to induce acceleration in cancer growth by Collier and Cohn. Leopold (1932) used

injections of sodium chloride and caused small cancers to develop on the tongues of rabbits. After preliminary wounding of their ears, injections of sodium chloride caused fibromas to develop at the lesions in rabbits.

Gram has removed precancerous warts with *lanolin* (sheeps'-wool fat), to which he had added either the carbonate or the phosphate of soda, in from 2 to 3 weeks. This isolated report is here mentioned.

Sodium exerts a markedly toxic effect on the heart, and it impairs the action of white corpuscles, as phagocytes, or devourers of bacteria.

MAGNESIUM

The salts of magnesium aid in the formation of the albumin of the blood, reduce foreign matter and waste, and maintain the osmotic pressure of the blood. Blood has about 3 milligrams in each 100 cc. of magnesium.

The chief storehouse of magnesium is in the bones. It requires the presence of calcium salts for its proper function and is injurious in the absence of calcium. An excess of magnesium in the blood is said to cause greatly increased sugar in the urine. Muscles and nervous tissue contain large amounts of magnesium.

Magnesium and Cancer

Katase found that magnesium favored growth of experimental cancers.

Marullaz, in 1930, was able to protect rabbits from developing tar cancer by administering magnesium chloride. And if the animals had already developed cancer, he found magnesium chloride inhibited further extensions of the growths. We might attribute to the *chlorine* these results.

Marchi, in 1930, made correlations between the high magnesium content of the water and the low mortality from cancer in the region around Moselle, France. Delbet, in 1931, reported the evidence of Tscherny, who, from his study in Algeria, showed that in 35 towns where magnesium was lacking there were 3 to 4 times as many cases of cancer as in the rest of the 104 towns compared. "Delbet's Salt," a combination rich in magnesium, calcium, and iodine, has been used as an adjunct to cancer treatment in this country as well as in Europe.

IRON

Iron is a requisite for the life of most forms of protoplasm. It is an essential element both of the oxygen-carrying *hemoglobin* in the blood, and of the chromatin substance in the *cell nuclei* which appear to control the most important and vital activities within the cells. Infants are born with a reserve store of iron, designed to supply growth requirements to the end of the nursing period, for human milk contains a very small amount of iron. The blood constitutes less than 7% of the dry weight of the body, but contains more than 70% of the iron. The human daily requirement of iron is about 12 milligrams. This is much higher during pregnancy and lactation. Iron deficiency is common also in the two critical periods of women, at puberty and at the menopause. *Anemia* and loss of weight may be the only symptoms of gastric cancer. Ewing cites cases of *gastric cancer* that were at first treated for pernicious anemia.

There is a close relationship between calcium and iron, for they are laid down in the same bony storehouses, together. Moreover, the excessive losses of calcium that characterize puberty, menopause, and pregnancy are also well known to be accompanied by iron losses and anemia. The author has identified such anemias with calcium-iron excretion. The relationship of glandular function is well shown by the fact that thyroid extract will often serve as an almost indispensable adjunct to iron therapy in anemias. Moreover, liver extract is in itself a thyroid stabilizer, and liver extracts contain iodine, iron and calcium.

Davidson of England has shown that when calcium is low, anemia will occur on the same intake of iron that will be sufficient to preserve the normal blood level of hemoglobin, if calcium is also present. Calcium is an iron-sparing agent. This is indirectly due to the fact that in excess, or too small amounts, it causes goiter, with heavy losses of both calcium and iron, and resultant anemia.

Cancer and Iron

Let us first consider the rôle of iron as supportive medication in cancer. In the cancer patient there has been such defensive action of the glands that vast amounts of calcium and iron have been lost. We are familiar with the anemia that occurs in many cases of cancer.

Ahlbohm used large doses of *iron* to cure the "Plummer-Vinson syndrome," in which females exhibited *achlorhydric anemia*. (See page 130.) It is believed that this treatment will prevent many deaths from cancer of the mouth, pharynx and upper esophagus, which sometimes follow the anemia.

This writer discovered in 1928 that, after administration of a small amount of iodide of iron to rats on a Vitamin A-deficient diet, they were greatly benefited. This was due in part to the action of the iodine, which tended to stabilize the thyroid gland. But, as we later showed, both the iron and iodine offset somewhat the injurious effects of excessive, unguarded Vitamin D. In 1930, Eder of California learned that iron added to cod liver oil was of great value in children (and adults) who had suffered from excessive sun exposure. He also found it valuable in treating freckles. This writer is responsible for the evidence that the iodine of cod liver oil is essential to its value in vitamin relationships. The unsaturated and saturated fatty acids and sterols of cod liver oil are nicely combined with iodine, so that speedy normalization of the glands of internal secretion will come in goiter, and in several vitamin deficiencies where glandular derangement has followed losses of fats. Liver extracts furnish iron, calcium and iodine, and they also normalize glands controlling these elements.

Douglas-Webster, of London, used liver extract intramuscularly in *radium sickness*. Anderson has supplemented it with iron and Vitamin B, and secured excellent results. Iron and iodine will aid in offsetting radiant energy injuries, and iron added to cod liver oil will provide thus the calcium, iron and iodine that the "parasitic" cancer itself causes to be excreted, and that radiant energy causes to be eliminated even more rapidly. (See page 141.) The iodine of cod liver oil prevents its fats and lipoids from causing physiological disturbance, characteristic of "unsaturated" substances in excess.

CHLORINE

In the body, chlorine is an extremely necessary element. In the blood and body fluids, it unites with sodium, as sodium chloride. In the gastric juice, it forms hydrochloric acid, an essential to digestive action.

Chlorides are extremely powerful agents in the destruction of bacteria, especially as combined by von Behring with iodine. The action of iodine-trichloride is now understood more thoroughly, since we know the chemistry of the *coverings* of bacteria, which are unsaturated lipoids.

In cancer cases, clinicians have for many years noted an early loss of gastric hydrochloric acid. Moore and Palmer, in a series of malignant and non-malignant tumors, found that nearly all exhibited a decrease in gastric HCl. They attributed this to a reduced amount of acid ions in the blood.

Deficiency in gastric secretion means calcium and iron deficiency, and as a result toxemia from intestinal putrefaction develops. This picture of disturbed nutrition is also the picture seen in early stages of cancer.

The presence or absence of calcium depends on the acidity of the intestinal tract. In the upper part of the small intestine, an acid medium renders calcium salts soluble and promotes their absorption. In an alkaline medium, insoluble calcium salts are formed.

Ahlbohm found that achlorhydric anemia (absence of hydrochloric acid, with anemia) preceded in women the development of cancer of the mouth, pharynx, and esophagus. Early loss of teeth, soft spoon-shaped nails, and a dryness of the mucous membrane of mouth and tongue were other signs. Ahlbohm was able to correct the condition by administering hydrochloric acid, with iron, and to treat incipient cancer successfully thus. We are led to the thought that some cases of "anemia" were cancer.

It is worthy of note that Ewing of the Memorial Hospital, New York, cites evidence that in cancer not involving the digestive tract a similar deficiency in hydrochloric acid occurs. It is evident that a general influence is exerted by cancer, affecting gastric secretion.

This author believes that glandular disturbance is the key to cancer development, and that the relationship between deficient hydrochloric acid and the anemia of cancer cases is to be thus explained.

In 1931, Tashiro and Schmidt showed that *thyroid feeding* increased the susceptibility of guinea-pigs to the toxic action of bile salts, and the development of gastric ulcers. (See Vitamin deficiency, thyroid activity and gastric ulcers, page 77.)

We know from the investigations and clinical experience of Friedenwald and Morrison (1933) that emotional disturbance will cause excessive and eventually reduced hydrochloric acid in the stomach. Likewise, Cushing has shown how tumors of the midbrain or pressure due to operations in that region may result in perforative lesions of the esophagus, stomach, and small intestine. The writer has directly correlated this condition with the fact that iodine, released in excessive amounts, will stimulate the thyroid gland; and it has been demonstrated that the midbrain is the great reservoir for iodine, of the brain. Thus emotional disturbance which is known to increase the blood iodine from 20% to 50% may cause a release of glandular iodine and midbrain iodine, to stimulate the thyroid gland, cause irritative action of bile salts, and of chlorine and iodine on the delicate mucous membranes of digestive organs. (See Mental states and cancer, pages 233 and 234.)

We can go further and link a number of well-known causes of gastric ulcer with glandular overactivation. Worry, alcoholism, deficiency diets, as in Vitamin A deficiency which permits the action of salt mixtures, in animals not receiving protective fats; and tumors, or operative injuries affecting the brain, are all thus able to cause the initial thyroid activity, which is followed by lack of HCl, and even by the development of anemia.

We all know how emotional disturbance affects the digestive tract. But clinicians have recorded cases in which gastric ulcers have developed in patients who are chronic worriers. In many of these instances, treatment by special diets and prolonged rest do not seem to be of great value. But a change of scene, the relief from annoying conditions, or unexpected good fortune will induce rapid recovery.

Physicians report that the negroes are free from stomach ulcers because they do not worry. One colored man was asked why he did not worry. He said that when he sat down to worry he went to sleep instead.

Alvarez cites the case of a young woman who suffered severe gastric disturbance with pain when she learned that her mother had a cancer of the stomach. The mother was ignorant of her condition, and suffered no pain at all. The daughter *could* develop gastric ulcers from worry.

Chlorides and Cancer

Experimentally, Collier and Cohn found that the growth of rabbit carcinomas was accelerated by sodium chloride. Leopold, in 1932, used injections of calcium chloride and sodium chloride and caused papillomas to develop on the tongues of rabbits. Rondorf, in 1933, was able thus to produce papillomas on the rabbit tongue with calcium chloride, glycogen and cholesterol.

One of the oldest escharotics used for cancer is *zinc chloride*. It has been used in pastes for many years with remarkable success.

Marullaz and Delbet, in 1930, have used magnesium chloride injections to protect rabbits inoculated with tar cancer; if the animals had already developed cancer, the growth extensions were retarded.

Dr. Bertha Van Hoosen for some years had used emetin hydrochloride with benefit in human cancer cases. Emetin hydrochloride is a well-known remedy for parasites, and undoubtedly acts on the glandular mechanism.

Dr. W. B. Guy, well known to clinicians for his use of hydrochloric acid in various diseases, has found that a combination of HCl and benzoic acid will benefit some types of cancer. He describes (1935) cases of breast cancer, esophageal cancer, and of cancer in the region behind the nasal passages. All of them showed marked improvement after the acid therapy. (See *Medical World*, November, 1935, p. 720.)

Guy administers hydrochloric acid, combined with potassium and arsenic, in preliminary treatment of cancer. He also applies sodium iodide, injecting it intravenously. In 1935, Guy reported using hydrochloric acid and potassium, and following it with oral iodine. Thus he was able to control irradiated cases and to prevent metastases. His work has been followed by certain clinicians, who approve of the combined action of chlorides and iodides, which tend to balance each other in the tissues.

Chlorination of Water

Realizing that chlorides stimulate the thyroid gland and cause experimental goiter, we may very well consider the fact that a variety of diseases that involve premature old age (including cancer) could develop from the use of city water that has been heavily chlorinated.

Colonel M. J. Blew of Philadelphia has for several years been much interested in this possibility, which should be tested.

Man is the only animal that takes sewage, and by treating it with poison considers that it is rendered potable, if not palatable.

IODINE

Iodine is one of the most important elements in the human body. A small amount of iodine is all that determines the difference between an intelligent person and an imbecile. In the body fluids, iodine aids in their defense against bacteria and accumulated wastes. All cells and tissues are activated by iodine, and it is an essential element in every one of the glands of internal secretion. Iodine in small amounts is known to accelerate growth in animals and plants. It has also been proved to stimulate growth of experimental cancers, and tissue cultures of glands, if in minute amounts; but in larger percentages it stops their growth.

Iodine Content of Animals Used for Food

(From McClendon's "Iodine and the Incidence of Goiter,"
University of Minnesota, Minneapolis, 1939)

<i>Animal</i>	<i>Locality</i>	<i>Dry</i>	<i>Iodine in decigrams per kg.</i>
Clam	U. S.	D	6,200
Mussel	U. S.	D	4,368
Oyster	U. S.	D	6,000
Scallop	U. S.	D	5,048
Lobster	U. S.	D	11,590
Shrimp	U. S.	D	2,250
Codfish	U. S.	D	5,350
Codfish	Norway	D	29,340
Haddock	U. S.	D	24,070
Mackerel	U. S.	D	1,280
Mullet	U. S.	D	20,490
Salmon	U. S.	D	1,559
Sardine	U. S.	D	1,510
Sturgeon	U. S.	D	1,539
Herring roe (canned)	U. S.	D	3,790
Shad roe (canned)	U. S.	D	4,100
Cod liver oil—refined	U. S.		3,590–14,940
	Scandinavian		5,100–7,200
	Scottish		9,100–16,500

Iodine in Salt Springs

While we have not discussed sulphur in our list of important elements, it has long been known that calcium sulphide is specific for boils, and is of great value as a tonic.

The presence of 1600 gamma of iodine in the hot sulphur springs of California, and of considerable amounts of iodine in other salt springs, emphasizes the combination of lime and of sulphur with iodine in such waters.

For about 50 years the pharmacopeia has listed the high iodine content of numerous salt springs at health resorts all over the world. These springs have been frequented by syphilitics and persons afflicted with rheumatic difficulties. Glandular derangement is a forerunner of arthritis, and the value of iodides in syphilis has long been known.

Carlsbad, Vichy, and Saratoga Springs are well-known locations of health resorts. Lorand of Carlsbad has for thirty years directed attention to the importance of thyroid derangement in diseases.

Deep wells furnish adequate iodine to the wise old residents in goitrous regions. The writer was impressed with the good sense shown in a University town (Morgantown, West Virginia) by the vigorous men of 75 who walked a half mile to secure deep well water. Their less healthy sons used chlorinated water.

Iodine in Plants

The marine algae contain a higher percentage of iodine than any other known food substance. The large coarse brown kelps, when dried, were shown by Tressler and Wells to contain 900,000 parts of iodine per billion.

The Japanese use 6 or 7 different kinds of seaweeds at a single meal. Seaweed gelatin, called "kanten," is sold as commercial agar-agar, and used to relieve intestinal stasis.

The iodine in seaweed varies with the part of the plant used; the stem contains even more iodine than the leaves. Iodine content decreases with the age of the seaweed, being highest at the time when maximum growth takes place.

Kelp is furnished by several firms in the United States and Canada, in tablets, and also in powdered form, suitable for use instead of table salt. It contains in natural balance iodine, iron, copper, calcium, phosphorus, magnesium, sulphur, zinc, sodium, potassium, aluminium, and chlorine. It is an excellent source of Vitamins A, B and D. Fresh kelp contains Vitamins C and E also.

Water cress is a fresh water plant that was identified as iodine-rich by Chatin in 1850. It is an excellent source of Vitamins A, B and C, and used in diabetes as a folk remedy.

The South Carolina investigators (Remington and associates) have shown that iodine appears in plants of the "Iodine State" as follows:

<i>Food</i>	<i>Parts per Billion</i>
Broccoli	1,603
Lettuce	912
Spinach	694
Cucumbers	523
String beans	429
Egg plant	338
Turnip	223
Potato	211
Strawberries	181
Onions	136

In goitrous regions the iodine can be increased in plants, and in animal food products by soil fertilization, and by using iodine and kelp in the rations of animals.

Yeast, hops, parsnips, radishes, beets, carrots, and turnips have been stimulated to increased yield by kelp or iodine fertilization.

Alway and McClendon increased the iodine content of alfalfa 300 times by iodine fertilization.

In Stoklasa's studies, he learned that in sugar beets iodine produces more rapid germination of the seeds and formation of the chlorophyll, and that resultant plants are larger.

We have elsewhere discussed the fact that the youngest seeds of wheat and other sources of Vitamin E contain highly unsaturated fatty acids. They absorb iodine as they grow, and finally cease growing. We have correlated this with the chemistry of cancer growth.

The outer layers of grain are much richer in *iodine* than inner layers. This condition may be directly correlated with the vitamin deficiency diseases, in which removal of the outer layers of rice and wheat causes degeneration of nerves and general debility in persons who eat them exclusively. This is linked with glandular imbalance. Vitamin B is beneficial in paralyses. (See Vitamins, page 86.)

Plants grown on soil enriched with iodine will, when fed to cows, cause more regular sex cycles, a higher milk yield, with greatly reduced bacteria, and will prolong the lactation period. Contagious abortion and mastitis have been stamped out in herds of cows thus fed.

Lund, by feeding seaweed to cows, increased the iodine in their milk from 30 to 3230 gamma per kilogram. W. W. Kincaid, by kelp feeding, was able to increase the milk production of his herd greatly, and one cow showed a 150% increase in butter fat over the two preceding years.

Iodine feeding increases the egg laying of old hens, and also increases the number of eggs laid by young birds as much as 25%. Iodized eggs have been used in goiter, arteriosclerosis, and anemia, as reported by Zickgraf.

This author is in favor of furnishing eggs from iodized fowls to the public generally, to offset possible injurious effects of their unguarded cholesterol, for cholesterol feeding causes arteriosclerosis. (See page 109.)

Iodine and Cancer

As one of the most valuable antiseptics, iodine has been used for many years in medicine. In 1922, Sajous reported that *iodine destroys tissues of low vitality*, and simultaneously excites healthy tissues to greater activity.

In 1908, Van den Welden found that potassium iodide diffused readily into cancer tissue. And in 1912 he found that cancer cells have a selective affinity for introduced iodine. Weil reported in 1916 that necrotic areas of cancers contain more iodine than other tissues, after its intravenous injection.

That iodine is absorbed by *growing cancers* from surrounding tissue is indicated by the studies of Currie who, in 1922, reported that

analyses showed that the tissue fats close to cancers have a higher iodine number (indicating less iodine in them) than the fats in other parts of the body.

When the thyroid becomes cancerous, and sends off metastatic or dispersed portions of itself, it can be identified by its cellular structure. For example, Plaut has recorded thyroid tissue in ovarian cancers, which he analyzed for iodine, and later tested with tadpoles. It was iodine-rich and caused metamorphosis of the frogs. Masson and Mueller studied six cases of ovarian cancer, in which they likewise identified iodine-containing thyroid tissue.

Holler, in 1923, learned that cancer tissue was rich in iodine at the time when the tumors were breaking down. He attributed the affinity for iodine to the secondary inflammatory changes in the cancers, but did not draw any conclusions regarding the power of the iodine to break down growths.

Tissue cultures of chick heart muscle were stimulated in growth by a 1 to 100,000 dilution of thyroxin, in tests made by the Japanese Dr. Sato, in 1930. Sato found also that in a 1 to 500,000 dilution, thyroxin accelerated the growth of cultures of chick myxosarcoma, or muscle cancer. Thyroxin contains about 65% iodine.

In 1933, McCarrison, the distinguished officer in the Indian Medical Service, who has done so much research on the vitamins, reported tests with tissue cultures of the thyroid gland, which were accelerated in growth in different degrees according to the strength of concentration of sodium iodide introduced.

Murohara, in 1930, was able to accelerate the growth of transplanted rabbit carcinoma by injections of small amounts of thyroxin, while larger amounts prevented the growth of such transplanted cancers.

Dietary iodine in very *small* amounts, or in *excessive* amounts, proved to be injurious, or ineffective, in tests made by Sugiura and Benedict. In their experiments with rodents, in 1935, abnormally high or insufficient iodine caused a slow regression of existing cancers, and there was a very high percentage of "takes" of implants. On the other hand, a *normal amount of iodine, sufficient to prevent goiter*, prevented implants from producing cancer, and caused regressions of existing ones.

Matsuoka, in 1930, used potassium iodide to retard the development of rabbit sarcomas and prevent their metastatic spread. He found that the implantation of thyroid gland acted similarly, but that if the thyroid of the experimental rabbits was removed, growth of the tumors was accelerated.

Mellanby, in 1938, reported that iodine produced the inactivation of the Rous chick sarcoma.

For some years prior to 1925, Botelho treated inoperable *human cancers* of the face with a salt solution containing glycerin, tannin, potassium iodide, and iodine. His success was reported by E. F. Smith, who has studied plant cancer.

Lead iodide has been used in Europe and the United States with some degree of success in human cancer. It was a featured treatment by Blair Bell, about 25 years ago. In the treatment of "utterly hopeless cases of cancer," the *Lancet* for Feb. 9, 1924, stated that Dr. Bell's results were encouraging.

Irradiated Iodine

There are important reasons for considering that irradiation influences the iodine of a tumor, and makes it more efficient. Recently, X-ray irradiation has been used to release *nascent iodine* from non-toxic compounds that have been injected into affected areas. Emphasis has been laid on the bactericidal action of such liberated iodine, and the evident correlation with the action of X-rays and radium on cancer-iodine has been for the most part overlooked.

For some years, Bourignon and his students in Paris have used electrical means to cause the release of ionized iodine in the treatment of cancer. In 1922, Botelho reported that he had removed scars by the electrical release of iodine from potassium iodide; in treatment of cerebral tumors, electrical action on calcium iodide proved effective.

Lieben and Kraus, in 1931, showed that iodine is released from organic combination in the thyroid by X-rays and by ultra-violet light.

Sperti and Norris, in 1928, found that in experimental mice the action of X-rays on their cancers was very much increased by the presence of caesium iodide in the tumors.

Ernst, in 1932, described his use of an iodine compound in many cases of human cancer as an adjunct to irradiation with X-rays or radium. He cured 40 out of 54 cancer cases thus.

At Hahnemann Medical College, Philadelphia, a distinguished radiologist of long experience, Dr. Frank Benson, has used *colloidal iodine* for 15 years in the treatment of cancer. He has records of more than 60 cases of rectal cancer thus treated successfully. He permits me to make the following quotation, "In advanced and disseminate cancer, the use of certain colloids may bring about a limited change in the malignant status, but only when the colloids are of an anionic character." He also states, "You can see that my idea is not based upon the use of irradiated iodine, but upon the fact that an anionic colloid of iodine is a carrier of electrons, which are attracted to the malignant cells (which have a changed polarity), and that this method has the great advantage of being used systemically."

Dr. Benson began our conference by stating that he had not only used radiant energy in combination with iodine, but that he had records of success in cases where iodine alone was used. He had long appreciated the fact that the anionic colloid of iodine exerted an influence comparable to radiant energy in breaking down tumors. Truly, "facts are stubborn things."

Masked Effects of Irradiated Iodine on Cancer

When clinicians irradiate glands that are sources of iodine, and thus cause cancer regressions, they are not aware of the physico-chemical action. For this writer has been first to clarify the matter of iodine action in the glands of internal secretion.

Professor E. Gley, in his book on "Internal Secretions," in 1917, stressed the fact that, with some preparations from glands, the characteristic physiological effects could only be obtained by doses so excessive that they represented in weight the masses of several such glands. He naturally believed that a common element in all the glands was the one that caused the beneficial effect. And he asked, "Is it not plausible that this action depends on the presence of a substance which occurs in all these extracts, consequently a substance that is widely distributed and therefore more general than specific."

After twenty years of research with fresh and commercial glandular extracts, we discovered that the substance common to glands of internal secretion is iodine. And this author has discussed its distribution and functions in an extensive series of articles in medical and scientific journals. (Consult Chidester, "Tumor iodine and the influence of radiant energy on new-growths," *Medical World*, vol. 53, No. 4, pp. 234-235, 1935; and "The relation of iodine to the effectiveness of endocrine extracts," *Archives Internationales de Pharmacodynamie et de Thérapie*, vol. 48, Fasc. III et IV, pp. 354-365, August, 1934.)

When Keegan of Philadelphia used irradiated blood in the successful treatment of human cancer, he chose the blood of *pregnant women*. As we have emphasized, such blood is exceptionally high in iodine. (See page 153.)

Counsellor, of the Mayo Clinic, in a discussion of the influence of the ovary on the incidence of breast cancers (1936), cited cases where doses of X-rays used to cause ovarian degeneration and menopause were effective in causing the disappearance of metastatic tumors from the lungs. He also reported metastatic cancers of the prostate gland that disappeared when sterilizing doses of the roentgen rays were used on the testes. Prostatic hypertrophy has been treated with iodized ointments successfully for 50 years.

Hoffman, in 1933, described the results of irradiation of the ovaries, followed by disappearance of metastatic nodules in the breasts. The ovaries are rich in iodine. (See page 188.)

Irradiation of *any* gland or structure in the body that *contains iodine* will send into the body fluids activated iodine, which can exert its carcinolytic power, and break down cancers, wherever it passes. Whether the activation of potassium, sodium and other liquefying elements that are radiated easily will be of such great value is to be determined.

In his report of about 5 years ago, Failla, of Memorial Hospital, New York, says, "All that is needed is a substance which is retained by cancer tissue to a larger extent than the normal tissues and organs of the body. By itself, this substance may be perfectly harmless and without effect on the cancer. However, it could then be made artificially radioactive, or it could become a carrier of radioactive matter.

The radiation would destroy the tumor, without injuring unduly the normal structure."

This author has pointed out repeatedly that (1) the necessary cancer-destroying substances exist in small amounts in cancers, and are activated by present methods of radiation, when it is not excessive; (2) that, even without radiation, some tumors regress "spontaneously" because of these carcinolytic substances, gathered from the blood and lymph; (3) that the existing unorthodox methods of treatment by diet and glandular therapy will *mobilize*, for effective use, iodine and other elements that are valuable in causing cancers to break down, and *prevent* further spread of the growths, and even will *offset* possible injuries from excessive radiation; (4) sunlight, acting on the foods, and on persons, in proper amounts, will activate iodine and aid in producing vitamin and gland balance which protects against cancer, anemias, and vitamin-deficiency diseases.

Irradiation, by causing the more effective action of iodine on cancers, may be extremely beneficial. But heavy radiations, like other beneficial agents which break down malignant growths, may cause them to spread by metastatic dispersal. And heavy radiations will drive away calcium, which is important in limiting the speed of cellular breakdown and thus preventing metastases.

The amount of iodine that can be used after radiations is found to be considerable. An able clinician who asked this writer to investigate his method of treatment a few years ago was fearful that a medical journal report of the size of doses of iodine used on radiated cases would arouse other physicians to protests. This doctor, in charge of a hospital near one of the largest cities of the country, had been pilloried by his colleagues, and attempts had been made to disbar him from practice, because he dared to take "hopeless" cases that had been given up after they had been operated upon, and treated with radium and X-rays. He used a number of drugs that the general run-down condition of his cases seemed to require. And one of them was iodine.

This writer arranged a conference with one of the nearby Directors of a Research Institute, and the doctor told of his method. When he came to a supposedly startling account of huge doses that were necessary in giving iodine to irradiated cancer patients, the Re-

search Director said, "Why, Doctor, I think that is not alarmingly high for iodine." He called for certain reprints, and showed my friend that several years before he had used doses of 20 times the amount of iodine, himself, in another disease.

Examination of case records and affidavits showed why this harassed doctor was able to continue in practice, despite the bitterness of some of the intolerant or jealous physicians in his medical societies. He had succeeded in prolonging the lives of many patients, who had been given up to die by others. A certain religious group had given him medals until he had a large boxful, which he showed me. And the prayers of such grateful patients and their friends did a great deal to assuage the grief of this noble man that his ideas and methods were not appreciated. His medication cost the patient a few cents a week. Many cases were "charity." He was another of those able doctors who placed service above money; and human lives above the adherence to a fixed rule for treatment.

No one who is unprejudiced would consider that surgery and radiation have solved the cancer problem; for surgery relieves only the local cancer; and radiation can merely introduce a factor which in itself is known to be cancer inducing, and of doubtful value in some internal cancers.

While the writer was studying the technique of mouse cancer, and attempting to learn something about the action of iodine and other chemicals on spontaneous and implanted cancers in animals, at a University laboratory, a colleague decided to look into the possibility of securing, for our use, tumorous animals from the general animal colony which supplied all the scientific departments.

It was with great amusement that we learned from the animal-keeper that he could supply no cases of tumorous animals. "Why," said he, "we rarely have cases of tumors in our stock, and when we do, I immediately paint them with iodine, and they go away."

One of the ablest clinicians who used iodine in cancers was in his early years a veterinarian. He learned from such practice that tumors were easily removed in horses and cows by iodine applications.

We have mentioned the radio-activation of iodine as the explanation of what happens in connection with cancer regressions, after X-rays or radium treatment. Bishop of the Sydney, Australia, Can-

cer Commission has said, "Iodine in the organism may be for the purpose of capturing radiations, and the consequent liberation of electrons."

Of the 12 elements tested by Frazier and Glaser, at the University of Pennsylvania, iodine was the most successful in shadow-casting capacity when exposed to X-rays. Treatment of certain diseases of the respiratory tract, after iodine in oil has been used for the purpose of disclosing the condition of the tissues by an X-ray picture, would be more successful just because of the original iodine in use. Iodine breaks down fat-like coverings of bacteria.

At the Memorial Hospital, New York City, a 1944 report indicates that radioactive iodine is now being used to locate metastases from thyroid cancers to the skull. We have already described the work of Bourignon, and of Benson, with activated iodine.

The radiation laboratory of the University of California has been able to liberate from bismuth sufficient amounts of the new rare element number 85 for experimental purposes. This element, called "eka-iodine," is a close relative of iodine, and gives off radioactive particles which travel short distances in tissue. In the thyroid gland they travel about $\frac{1}{500}$ th of an inch.

In experiments described at the August, 1940 session of the National Academy of Sciences, Drs. Hamilton and Soley, of Berkeley, show that the thyroid gland absorbs and retains "eka-iodine" just as it does iodine.

The value of this new element, made available by the atom-smashing giant cyclotron, may exceed that of ordinary iodine in cancer, as well as in specifically thyroid diseases. Its potential value in breaking down lipid accumulations is almost unlimited. Not only may it cause the destruction of tumors, gallstones, cataracts, and atherosclerotic plaques, but this writer believes that it may break down the coverings of bacteria and the organisms of syphilis and leprosy even more effectively than the less strongly radioactive ordinary iodine. We have possibly reached a new era in immunization and therapeutics.

CHAPTER IX

Radiant Energy: Its Benefits: Its Hazards

In an address to the American Radiological Society, Soiland of California issued a warning against the use of radium by untrained persons. There are about ten grams of radium constantly for rent in the United States. Many of the persons who rent radon seeds or needles are inexperienced, and correspondence courses cannot furnish the information which they should have. Practical work with able radiologists, in clinics, should precede any licensure to use radium or X-rays. It is well known that internal cancers are not likely to be subjected to radiations without injuring soft tissues. And radiation near bones causes their destruction. Yet we find a few radiologists who continue to cause rapid breakdown of jawbones and pelvic bones. And such bunglers leave implants of radium for months to do their awful work, while experts favor a few days of such treatment at most.

Dr. L. Bothman (1939) of Chicago has warned us that *glaucoma* with loss of vision may follow large doses of X-rays or radium used in treatment of cancer of the cheek or tumors of the eye.

Certain specialists in "beauty clinics" have in the past been guilty of producing cancer of the skin by the use of X-rays in hypertrichosis. Dr. Leborde of Paris describes such a case. A woman was treated for excessive growth of the hair on her face in 1910; the hair was killed, and all seemed well for about 3 years, when the skin and border of the lips showed radio-dermatitis. This was followed by cancer of the upper lip.

Finsen, in 1903, reported the appearance of carcinoma similar to X-ray cancer on the site of lupus that had been presumably "cured" by X-rays. Bone sarcomas have been experimentally produced in rabbits by implants of radium.

The 48 cases of radium dial painters who died a few years ago, and whose successfully waged suits to recover damages brought their

plight to our attention, serve to emphasize the production of bone lesions by radium.

In 1931, Sir George Lenthal Cheatle, of London, reported that he found radium worthless in the treatment of mammary cancer. He used it in the treatment of cancer of the tongue.

Dr. F. C. Wood, of Crocker Institute, Columbia University, New York, stated in 1931, "High Voltage X-rays are no more effective in killing individual cells than any other X-rays." Packard, of the Crocker Institute, a student since 1914 of the effects of radiation with radium and X-rays on animal cells, has warned us of the importance of using accurately measured doses of radiant energy.

The writer has published a communication from Dr. Hal Bieler of Pasadena, Cal., who noted from case histories 10 laryngeal cancer patients that came to autopsy with completely degenerated thyroid glands. They had received heavy doses of X-rays. (Cf. Chidester, "Tumor iodine," *Med. World*, 53, 234-235, April, 1935.)

There is some argument over preoperative radiation, since there are regions in which such treatment may cause the breakdown of metastatic portions of the cancer. Sir John Fraser, of Edinburgh (*Edinburgh Medical Journal*, 1939), in discussing his treatment of cancer of the breast states, "Preoperative deep X-ray treatment seems to be illogical and even harmful." Fraser uses postoperative X-ray treatment as a means of reaching malignant cells that have extended beyond the area accessible to operation.

The distribution of essential chemical elements is regulated by the glands of internal secretion, the body fluids, the emotions, and by physical factors including temperature and radiant energy. Applied as a remedy, *radiant energy*, including ultra-violet light, X-rays and radium, will *regulate the dispersal of chemical substances*. Its action must therefore be considered much more significant than that of a mere cell or tissue destroyer.

Reding, in 1929, found that X-rays benefitted the sugar mechanism and restored calcium in the blood of cancer patients. Here we have direct and indirect effects involving the glands of internal secretion in cancer control. For radiant energy activates the calcium controlling glands, and normalizes the burning of sugars.

Experimental studies by Rondoni have demonstrated pronounced

increase in the size of tumors following the injection of sugars into sarcomatous mice.

On the other hand, Professor Dr. Gomes da Costa (Lisbonne), 1931, has found that insulin intensifies the action of X-rays on the oxygen-reducing capacity of muscles and cancerous tissue. (See page 144.)

Klaus, in 1939, raised the *serum cholesterol* of cancer patients by radium and X-rays. Low cholesterol is correlated with exhausted thyroid glands. The activation of *iodine* in the body by radiant energy could induce greater cholesterol dispersal and circulation, and might even indicate that the tumors were being broken down.

In the February 26, 1938, issue of the *British Medical Journal*, Doctor Percy Furnival of Devon, England, described the effect of excessive radiation on his tonsils. Later other doctors gave their experiences with patients. It was natural that letters in defense of radiation also appeared.

It seemed evident that radium causes edema, burns, and the necrosis of soft or bony tissues, even a total destruction of bones.

Dr. F. Ellis, Medical Director, Sheffield Radium Center, strongly advocated a "rational" radium dosage. He said, "The reason for radionecrotic ulcers is undoubtedly overdosage. I found no clinic in the United States, of many visited, where spacing and application of this principle of rational radium dosage were carried out."

From the British Isles we have an amazingly frank statement made by Sir Leonard Hill, the physiologist, in November, 1939. He said, "If all the radium in the country, buried for security from bombing in deep holes, remained there, the world would be little worse off."

Dr. G. G. Ward, of the Women's Hospital, New York, stated in 1933, "Correspondence courses in radium therapy are dangerous for the inexperienced. Radium is a two-edged sword and its use is far from simple. Larger doses than are required to destroy the cancer cells will destroy the normal structures, also, and produce extensive necrosis."

It has been shown that heavy and repeated radiations will result in later reactions, confused with recurrence of the disease. The devitalized structures ulcerate and are ready prey to infections.

Dr. John Swan, deploring the use of diagnostic X-ray machines by tyros, says, "What can we say of the physician who will undertake to give postoperative irradiation with Röntgen rays with an equipment suitable only for diagnostic purposes?"

The author has recently received a copy of Dr. J. E. Hett's new book, "Cancer, Its Causes and Prevention, and New Treatment," published in Canada in 1943. A pioneer in the use of X-rays in cancer, Dr. Hett reported in September, 1904 (*J. Advanced Therapeutics*), on the complete absorption of a large uterine fibroid of the uterus after X-ray treatment. But he has concluded that in general cancers are not local growths alone (like fibroids) but are outgrowths with a general cancerous condition in the system. He says, "The treatment of cancer by X-rays in cases of metastases is absolutely worthless, because terrible injuries can result."

Murphy and Norton found in experimental studies that an X-ray dose which produced an increase in the lymphocytes (blood corpuscles with large nuclei) in control animals was adequate to render 50% of animals immune to grafts of their own tumors, and to retard the growth of such tumors in the other 50%. The radiologists are not certain about dosages, but several different methods are being evaluated for different types of cancer.

Except in treating superficial cancers, the old method of applying a single massive dose, which is caustic and speedy in action, has been abandoned.

Fractional doses are applied frequently, until the total dose has been built up to a point that is considered optimum and effective.

Pfahler devised the "saturation" method. Beginning with a large initial dose, the succeeding daily doses, which are small, are continued until the total dose has been given. Holfeder has advocated similar treatment.

The well-known method of Coutard is fractional throughout. He starts with high voltage (at least 200 kilowatts) and heavy filtration (from 1 to 2 mm. of copper) and gives daily small "divided" doses over a period of about a month before the total dose is finally reached. This method has the great advantage of attacking the tumor cells, but enabling the normal cells to aid in the establishment of chemical support to the treatment.

Christie favors the use of copper filters that are at least 1 millimeter in thickness, for thus he secures results that are superior, without injury to the skin. He advises increased filtration and lengthening the time for the delivery of the total dose.

There may still be in use some of the harmful glass-enclosed "radon seeds." The older types of radon seeds are largely replaced by gold and platinum seeds. And the radium element is furnished in needles with at least 1 millimeter of platinum thickness protecting against injurious effects. Radium needles which contain approximately 0.3 milligram of radium per centimeter will deliver a dose of 100 milligram hours per cubic centimeter of tissue in *eight* days, according to Christie. Yet, this writer knows of cases in which radium needles have been left for months adjacent to the jaw bone, in a futile attempt to do "something."

Christie stresses the fact that it is dangerous to *traumatize* cancer tissue. He says, "The disease may be disseminated just as certainly by the traumatism produced by insertion of the radium needles as by cutting through the tissue with a knife." Thorough irradiation by X-rays is essential before insertion of the radium needles. And dosage throughout the cancerous area should be uniform, by regularly distributed needles.

It is not surprising to those who have followed the history of the pathetic cases of radium dial painters, whose bones degenerated, that the radiologists find that in malignant bone cancers irradiation has made little headway. It is in the treatment of skin cancers that local effects are seen after irradiation. And *sunlight* converts some pigmented moles into cancers!

Since 1933, at the Memorial Hospital, New York, the Haublein method of continuous irradiation with low voltage X-rays has been used in certain types of cancer involving the blood and lymph-glands. It is continued for as much as 20 out of the 24 hours in a day, for several days at a time.

In the treatment of certain highly resistant forms of external cancer of the mouth, pharynx and larynx, Dr. Max Cutler of Chicago (1944) has originated a "method of concentration" by which the core of the cancer is irradiated with relatively strong doses. Exposure

is found to be effective without the danger of injury to adjacent healthy (and less resistant) tissues.

The writer has no information regarding the extent to which radiologists have used this technique. Concentration of strong radiations at the core of cancers was in use in 1936 in the hospital of Doctor Charles Whelan of Boston.

About 20 years ago Bouchard of Paris injected fluids containing radium emanations into animals, and at the autopsies learned that the radium emanations had accumulated in the glands of internal secretion, especially in the adrenals and the spleen. The spleen is primarily a blood-forming organ, with the function of forming new red corpuscles in the embryo and of aiding in the production of white corpuscles in the adult. The *spleen* is engorged with blood at every mealtime.

Physiological conditions are induced by radium emanations, when they are not too heavy, similar to those induced in animals by feeding thyroid extracts. We have already commented on the fact that radiant energy will activate iodine, which is generally distributed in the blood, lymph, and in all cells and tissues of the body.

Not only does excessive application of radiant energy cause local irritation and chemical disturbance, but it induces overactivity of glands of internal secretion, already disturbed by the cancer. Losses of essential elements ensue, and the general resistance is weakened.

Moderate radiations, with supportive medication and adequate foodstuffs, can aid in the necessary restoration of body functions, and the conservation and use of the chemical elements which destroy toxins and prevent abnormal cell growth.

We have shown how irradiation, plus chemical adjuncts, aids in cancer. Iron, iodine, and calcium are all lost from the body during the defensive action of the glands of internal secretion in cancer, just as in pregnancy. Iron and iodine are known to offset injurious effects of radiant energy. Quimby, in 1922, advocated iodine to radiologists for its protective effects. This writer experimentally showed and reported (1928) how iodide of iron in small doses offset excessive Vitamin D. Since 1930, Dr. H. Eder has used iron with cod liver oil to treat children who had received too much sunlight. As we have shown in numerous articles cod liver oil with considerable (natural)

iodine is best in vitamin deficiencies. We have also by courtesy of two drug firms been able to furnish our clinical groups with our own preparation of cod liver oil containing considerable ferrous iodide. Older drug firms who have marketed such iodized oils have by no means appreciated their value. Alert pediatricians and obstetricians are known who have regularly administered them with success in regions where cretinism and mongolism might otherwise appear in children. Our own independent research clarified the relationship of iodine to the vitamin-mineral-gland complex.

CHAPTER X

Sera

The blood bathes all cells in the body, bringing to them nutrients and carrying away wastes. In the nuclei of the white corpuscles, we have important conveyors of elements which attack bacteria. The glands of internal secretion pour into the blood and lymph their secretions, which are known to be of value in increasing immunity.

Bogomoletz first used sera from rabbits into which he had previously injected spleen and bone marrow extracts, and reported success in experimental cancer with them. Later, he prepared his "anti-reticular cytotoxic serum" by repeated injections of the cellular elements of human spleen and bone marrow into horses. This serum was found to decrease the resistance of animals to tumor transplantation (1936; 1939).

In recent publications (*Brit. Med. J.*, No. 4310, Aug. 14, 1943; and *Amer. Rev. of Soviet Medicine*, vol. 1, No. 2, Dec. 1943) Bogomoletz discusses the value of his anti-reticular cytotoxic serum in accelerating the union of fractures (O. Bogomoletz) and in infectious diseases of the nervous system including schizophrenia and psychoses (Mankowsky). The serum also improved cases of ulcers of stomach and duodenum, and eczema.

Bogomoletz found that "blocking" doses of a-c-s favored the progressive growth of carcinogenic transplants, but that *small doses* acted the contrary.

They stimulated the growth of the line of demarcation, activated the microphages, decreased the number of positive transplants, and even when a single dose of the serum was injected, had great prophylactic action against cancers. Pain was decreased in human cases, and metastases to the lymph glands disappeared.

The especially strong presentation of a case for the importance of increasing the reticulo-endothelial activity to counteract "new growths" in the important book by Stern and Willheim ("The Bio-

chemistry of Malignant Tumors," Reference Press, Brooklyn, 1943) is recommended for reading by all cancer workers.

We must comment on the fact that in the production of antitoxin for diphtheria, it was learned by Farrant (1913) that in horses that had deranged thyroid glands, the serum was of low antidiphtheritic value. The blood of normal horses contained *less iodine* than analyses of potent dried antidiphtheritic serum disclosed.

Rabbit-sera and horse-sera from animals that had been injected with spleen and bone marrow and had developed Bogomoletz's a-c-s would contain an excess of elements released from glands and other bodily storehouses in the defense processes aroused by such injections. Iodine is one of these elements known to be carcinolytic.

We have already discussed fully the remarkable work of Dr. J. E. Hett of Canada, with his *serum*. Dr. Hett's book "Cancer" is on sale, and the Provincial Cancer Commission of Toronto, Canada, is carefully studying his case records. (See page 44.)

Although he cites the report of Mountain and Dorn of the U.S. P.H.S., which gives the high cancer incidence in the Great Lakes region, in New York and New England (where goiter is so prevalent) and the low cancer deaths in South Carolina," the iodine state," Dr. Hett, like Mountain and Dorn, does not follow through to our own conclusions on goiter-cancer relationship. But he does emphasize *three essential factors* for cancer production. These are "irritation, ultramicroscopic germs (a virus), and an imbalance of the endocrine glands."

With Dr. Hett's conclusion that cancer is infectious, we cannot agree. Such agreement is not necessary in order to persuade Dr. Hett of the value of our supportive calcium, iodine, and iron, and it is not needed to insure our own belief in recorded improvements and cures of cancer with his serum.

Euglobulin, a serum from the blood of sheep, has been prepared by Dr. Thomas Lumsden, who reported in 1931 that it cured 74% of treated mice who had developed spontaneous cancer. Of the *cured* animals, 90% were resistant to reinoculations. The controls all died. In his subsequent report, in 1932, similar results with 80 mice were described.

Albert Wilson used serum from goat's blood in human cancers of the breast, with some degree of success.

We have mentioned the use of blood, but the most significant work that has been done with it is that in which radiant energy has increased the power of blood to break down cancerous growths. In 1935, Burton Hyde of Ohio reported his successful use of irradiated blood, which causes the regression of human cancers. He found that cancer of the urinary bladder responded to such treatment sooner than most types. He has used irradiated blood in dressings applied to external cancer, as well as by intravenous injections. The treatment relieves pain and prolongs life, but Hyde has thus far not furnished longtime records of *cures*.

In a personal report to the writer, Dr. A. Keegan of Philadelphia stated that, after mature consideration of its defensive qualities against disease, he decided that pregnancy blood would be suitable for irradiation purposes in cancer. For more than 5 years past, Keegan's records indicate the great value of irradiated blood of pregnant women in human cancer.

This writer has emphasized the fact previously (1934) that pregnancy blood is rich in iodine. Hoffman has shown that with 1 cubic centimeter of serum from pregnant women he could induce the same effect on the basal metabolism of rats as secured by 8 to 12 grains of thyroid extract.

The blood of young infants, also rich in iodine, was shown by Freund in 1910 to be about 21 times as powerful an agent in breaking down cancers as the serum of normal adults.

The great increase in iodine in the blood at menstrual periods, during pregnancy, and in the young infant has been previously discussed by this author in medical and scientific journals since 1933. The large amount of iodine in the blood will thus account for the value of extracts from the placenta (after-birth), the skin of embryos, and the umbilical cord, all of which prove effective in experimental cancer, and all of which exhibit bacteria-killing powers.

There may be a failure in some instances where blood is irradiated because of the lack in elements that are carcinolytic when activated. The research of W. Amberson of Baltimore on chemically prepared "blood substitutes" paves the way for an especially mixed combina-

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tion of the known elements which are cancer-destructive, before irradiation. It may also give us an accurate technique for the introduction of activated iodine, and prevent the injury now done by heavy irradiations. For such treatments now cause radionecrotic ulcers, and may cause delayed reactions, fatal in results. Distribution of activated elements through the blood and lymph is far safer and much more logical than the direct exposure of tissues to radiant energy.

In the practice of Magian, of England, where placental and ovarian extracts cause unsatisfactory reactions, he prepares a serum derived from the pooled blood of cancer patients. This mixed serum is in general use at some period of the treatment in all of his cases. It is aided by blood transfusions from healthy donors. (See page 189.)

"Good, the more communicated, the more abundant grows."

—MILTON

CHAPTER XI

Glands of Internal Secretion

"Perhaps a few prime principles which may conduct to much;
these last I offer."

—R. BROWNING

In 1912, this writer published a brief report of certain experiments with rabbits, rats, guinea-pigs and fowls, to which glandular extracts had been administered. Attempts were made to influence the pre-natal development of the most susceptible systems, especially the nervous system. Although the writer did not realize it at the time, he had paved the way for further studies which finally eventuated in his establishment of several principles regarding the glands of internal secretion.

Experimentation continued in this field until 1933, with the aid of postgraduate students, and the financial backing of funds at two Universities, and several outside grants. The final evidence necessary to determine the principles came from extensive correlations with the work of others, but the fundamental tests were made by our own group. Let us see what some of the most important findings were:

1. All the glands of internal secretion contain, at some time in their existence, considerable amounts of iodine. This is the element which is most concerned with the physiological effects that are common to all the glands.
2. All the glands of internal secretion, when active, control the distribution of calcium, fats, and fatlike substances.
3. The glands of internal secretion are closely linked with the so-called "vitamin" effects. Foodstuffs profoundly influence the glands and it is glandular derangements which are responsible for the definite symptoms of the vitamin deficiency diseases.
4. Gastric ulcer, cataracts, gallstones, arteriosclerosis, and cancer are all identifiable in animals that have been on a Vitamin A-deficiency diet. But the experimental evidence from vitamin studies is cleancut,

to show that thyroid derangement is responsible for every one of these conditions; and that when properly balanced with fats and lipoids, the iodine in Vitamin A-rich foods will aid in normalizing the glands and in restoring the animals to health.

5. Iodine in excess may cause sterility, and unsaturated (iodineless) fatty acids may cure it. But if unsaturated substances are given unguarded by iodine, there may be a condition of excessive thyroid activity, and excessive losses of calcium, causing rickets. Moreover, after the thyroid has been overactivated and then exhausted, investigators have even caused experimental cancer thus.

6. The evidence is conclusive that thyroid overactivity and ultimate exhaustion are related to the conditions which permit several types of cancer. Stocks, Chidester, Mitchell-Stevens, and recently McClendon have correlated the distribution of goiter with the occurrence of cancer.

7. Cancer of the thyroid, developing from adenomatous goiter, may spread by metastases to the lungs, skeletal system, lymph nodes of the neck and axilla, breasts, brain, liver, abdominal organs, and soft tissues. Ovarian cancers have been definitely identified as metastases from malignant thyroid glands, and the ovarian malignancies have yielded iodine as well as exhibited cell structure like that of the thyroid.

8. Irradiation of a cancer by activating elements in it causes their effectiveness in preventing growth to be increased if small divided doses are administered wisely. An adequate diet should support such radiations.

From the very earliest period of physiology, the idea of secretion has been identified with glandular organs. A gland is made up of one or more cells of a special epithelial type, which forms a product, the *secretion*. In glands with ducts, the secretions are poured out into collecting cavities, and pass to ducts, which transport them to the proper destination. Secretions discharged on mucous surfaces may be exemplified in the well-known salivary secretions. Gland cells may consist of a single layer, placed on a mucous membrane, or they may be coiled, as in sweat glands, or branched many times as in digestive glands.

The glands of internal secretion are of two types, (1) those with

ducts, and possessing secretions of value, in addition to the internal secretion, and (2) glands without ducts, and confining their function to the single type. The pancreas, which furnishes digestive juices as its external secretion through ducts, but which also yields *insulin*, as an internal secretion, from specialized cells, is an example of the endosecretory glands with ducts. The thyroid gland, which is able to furnish the important *thyroxin*, but which has no ducts, represents the other type. Ductless glands pass their secretions directly into the blood stream.

In 1775, Théophile de Borden, of France, believed that each organ was the source of a "humeur particulière" which exerts its influence upon the body generally. We have had similar expressions of the idea that special secretions were characteristic of muscle, brain, and other structures besides the glands. Muscle extracts have been tested and even compared with thyroid extract, in action, on strips of uterine muscles, with no realization of the high iodine content of muscle. Body muscles contain $\frac{1}{2}$ the body iodine.

W. B. Carpenter, in 1852, promulgated the doctrine that certain glands which he called "vascular glands" corresponded with ordinary glands in being able to withdraw or eliminate specific substances from the blood. But, he stated, "they differ only in being unprovided with excretory ducts for the discharge of the products of their operation." Carpenter included the present day "ductless glands," but he believed that the spleen and adipose (fatty) tissue were also to be classed with them.

As will be brought out later (pages 163-198), the thesis of this writer is that the glands of internal secretion, selecting essential elements, can only obtain them from the blood and body fluids. Thus there is not such a noteworthy difference between the various glands of internal secretion as some specialists in the behavior of their extracts would have us believe. It really is not surprising that the action of *muscle-extracts* on smooth muscle contraction should resemble that of thyroid extract, for *iodine* in each is capable of causing such contractions. In fact, one-half the iodine of the body is found in the muscles, while the thyroid gland contains only one-fifth.

Similarly, it is not to be wondered that calcium losses should follow the administration of large doses of any of the endosecretory

glands, for iodine separates fats from the calcium, and releases both in the blood. Iodized fatty acids are extremely important in the safe and effective transportation of iodine to the body tissues.

It is important that we recognize the presence in *insects** of fat-bound elements, which correspond to glands of internal secretion. Carpenter may not have appreciated the fact that fats and fat-like substances occur in the ovaries, the adrenals, and the parathyroid glands and that they aid in retaining the elements which constitute part of the "secretions" of these glands, but his conception of adipose tissue as possessing some qualities of the glands of internal secretion is thus not completely wrong. In medication with iodine, iodized fatty acids are reported to be the best available form, and rarely induce iodism.

The acceptance of the doctrine of internal secretions has come rapidly since the chemical preparation of adrenalin and of thyroxin. In 1889, Brown-Sequard described the results of experiments on himself when he was 72 years of age. He had injected subcutaneously extracts from the testes of animals, and noted marked rejuvenating effects. His report was ridiculed, and the results were attributed to auto-suggestion. But he undoubtedly had paved the way for the modern science of endocrinology. The facts regarding the safeguarding and sex stimulating iodine content of the testes and the ovaries have been ignored by the purveyors of cancer-inducing synthetic "sex hormones."

The glands of internal secretion, without ducts, from which came the term "ductless glands" include the *thyroid*, in which there are embedded the four small *parathyroids*; the *thymus*, found also in the neck region, below the thyroid, not far in front of the heart; the *suprarenals* are paired glands, well supplied with blood vessels, situated above the kidneys, in the body cavity; the *pineal* gland is in the dorsal portion of the brain, between and below the large cerebral hemispheres; and the *pituitary* gland is in the basal portion of the brain, behind the origin of the optic tracts from that region.

Glands of internal secretion with well-known primary functions include the reproductive glands, testes and ovaries; the pancreas; the liver; and, some authorities claim, the kidneys. We do not accept the

*Dr. R. Glaser of the Rockefeller Institute (Princeton) gave me this information in 1937.

kidneys in this category, but shall mention kidney extract, as it has been used in experimental cancer.

Besides these glands, it will be appropriate to mention the tests made in cancer with extracts from the spleen, and the placenta.

The striking results that have been secured by some experimentalists with extracts from the glands of internal secretion in spontaneous or implanted cancers among animals naturally attract our attention. Unfortunately, attempts to use glandular therapy in human cancer have not been so encouraging. However, this is due in part to lack of knowledge about the behavior and chemical constituents of specific extracts, and the proper means of supporting them, and even guarding their action.

Every gland of internal secretion is potentially a source of a cancer which may metastasize (spread) to other parts of the body. Witness the thyroid gland which, if it becomes cancerous, is able to metastasize to the lungs, soft tissues, bones, brain, and to other glands, especially the ovaries.

All glands of internal secretion are known to retain iodine in considerable amounts, in combination with proteins, fats or lipoids. The speed of release of the iodine in the parathyroid glands, or the ovaries, or the anterior pituitary gland, has a great deal to do with various body functions.

All glands of internal secretion influence the distribution of calcium, phosphorus, iron, iodine, fats and lipoids such as cholesterol. This means that derangement of their function, by operative removal of one of the chain, may alter bodily resistance to disease, and is, in some instances, directly responsible for illness.

The intimate relationship between the thyroid, the sex glands, and the mammary glands has already been pointed out. If tumors of any of the glands of internal secretion develop, this will influence all the others.

The blood and lymph bring to the glands of internal secretion the foodstuffs, which include proteins, carbohydrates, fats, lipoids, and the essential elements. The ability of these glands to select and to use properly the needed materials for health depends on a number of factors. First we must grant that *heredity* plays a part in determining the physiological activity of glands. Next, we must take into

consideration the possibility that *infections in the mother*, by deranging her systems during pregnancy, will influence the glands of the child. The rôle of *diet* during the formative years is significant, for upon the intake of proper foodstuffs depends the supply of essential elements, vitamins, and other materials which insure normal development and proper function of all cells, organs and tissues.

If we can strengthen the efficiency of our natural bodily defense mechanisms, and induce a normal flow of blood and lymph which will penetrate the tissues, we may be able to prevent wild-cell multiplication and cancer. It is known that *syphilis* and *old age* cause predisposition to the development of cancer after irritation. This is possible in part through their effect on the circulatory system.

Tar cancer involves a definite interference with the action of those substances which prevent lumps from accumulating. As we have brought out elsewhere, tar, and shale oil hydrocarbons are unsaturated, iodine-less substances. They absorb and thus overpower the elements that keep masses from accumulating around cells that have become clogged in their courses. The tar applications are chemical antagonists, and they seize and bind to themselves iodine, and thus interfere with the liquefying and distributing agents in the skin. It is well known that small amounts of iodine accelerate tumor growth in tissue cultures; and that larger amounts cause such tumors to regress. Iodine-binding tar, or oils, or fats will render the small amount of iodine that normally protects a given region incapable of functioning. The tumor once started will continue to grow by receiving various growth substances in the body. However, in tests with animals, and also with human cases, there is evidence that Vitamins A and E are able to aid in the defense against tar cancers, because they improve the functioning of those glands of internal secretion which furnish elements that control growth.

When we use glandular therapy, we are not necessarily substituting for a specific gland, but we may be supplying needed agents which will tend to normalize all of the glands of internal secretion. There is an intricate interrelationship between the glands, not only through the body fluids but also through the nervous system.

The proper control of glandular function depends on the basic factor of adequate nutrition. For elements, vitamins, fats, carbo-

hydrates, proteins, and fatlike lipoids are all related to the stabilization and efficient activity of these glands.

The value of sera; of artificially induced heat; of actual infections; of injected bacteria which produce fevers; of radiations which activate elements that stimulate glands; and finally of specific hormones, may all be shown to depend on the chemical condition of the body, and the proper functioning of its glands of internal secretion. Mental states are well known to influence glandular action, and so must also be taken into consideration. Chemical agents induce cancer regressions we know.

Operations that remove a specific cancer will also stimulate the defense mechanisms, and distant cancers may regress as a result, for *surgical procedures activate the glands of internal secretion*, and so do the *anesthetics* used during their course. Thus we can account for the regression of metastatic growths after operations, as induced by an outpouring of carcinolytic elements into the blood.

CANCER COMPARED WITH THAT OTHER PARASITE, A BABY

A cancer has been compared to a baby in its effect on the body. We know that there is a great demand for growth substances, and a natural stimulation to activity of organs in a pregnant woman. The growing cancer is also a parasitic structure, and it requires similar feeding, through absorption. The fats near a growing cancer are known to yield iodine and become somewhat desaturated by it. (See page 136 (Currie).)

The body supplies to the developing embryo and fetus its needed foodstuffs. These include proteins, carbohydrates, fats, lipoids, and the necessary mineral constituents. In pregnant women and experimental animals, cancers grow with great rapidity. This is due to the fact that the supply of elements which normally control both size-growth and the development of tissues and organs is shared by the developing child with the cancer. The cancer and the baby divide the essential elements, and the glandular mechanisms of the mother and baby both suffer. The growing cancers absorb and utilize in their own growth the important minerals and vitamins which are needed in the normal cell divisions and body growth of the baby. As a result of such robbing of needed substances, the fetus may develop

subnormally. On the other hand the cancer seizes essential elements, including iodine, and its amino-acids, fatty acids, and sterols will be furnished optimum chemical conditions for wild-growth.

The well-known Aschheim-Zondek test for pregnancy is one of the very first tests for cancer of a specific type. In the pregnancy test, the urine of a pregnant female has been found to exert strong action which stimulated the growth of the ovaries (female gonads) of immature, virgin mice. Certain investigators learned that in cases of carcinoma of the testis, the degree of malignancy was identifiable with the amount of the "gonadotropic" substance in the urine of the cancerous case.

However, this test is sometimes negative, and Melicow (*N. Y. State Med. J.*, vol. 40, p. 637, April 15, 1940) warns that its use may cause loss of time, and even lack of adequate treatment. We have not even mentioned this test in our section on "Diagnostic Tests."

In research work, it has been demonstrated that some rich foods actually stimulate the growth of cancers. Sometimes dietary restriction is beneficial. Starvation for a time removes from the body the excessive amounts of certain growth-acids which actually bind and interfere with the protective elements. It has already been stated that *starvation*, according to Willy Meyer (page 42), favors the tendency away from alkalosis towards slightly *acid* conditions, which he identifies with cancer regressions. Specifically, we know also that reduced intake of fats causes temporary overactivity of the thyroid gland.

Long before the writer became interested in vitamins, he ran experiments with various mammals in an attempt to influence their embryonic growth, by heavy doses of thyroid extract and several other glandular preparations. The experiments, begun in 1912, led to a study made in 1918, at the Wistar Institute, with rats. The pregnant rats were tested with thyroid extract and Kendall's newly developed thyroxin, and, after being fed heavy doses, none of them developed their young to maturity. Autopsies showed that these females with a previous history of fertility had started to develop their young but, under heavy iodine dosage, they were *re-absorbing them!* The Director of the Institute stated that similar results had been obtained with some foods.

It was not until the development of the work on Vitamin E that this writer came to a realization of the significance of his study with glandular extracts. For the removal of *fats* from the diet and the administration of salts that are known to cause thyroid overactivity occur in Vitamin E deficiency. Then it is that there results the same sterility, and reabsorption of embryos, that we had produced with thyroid extract.

If a *whole embryo can be reabsorbed* because of glandular activity, it seems logical to compare this process with the *regression and reabsorption of cancers*, resultant on a similar glandular action. This leads us to the manner in which glandular extracts are able to function, by means of their specific elements and known rôle of glandular stimulation.

Just what glandular therapy does to cancerous patients depends in part upon the method of administration; it also depends on the chemical condition of the patient's organs and body fluids; and it is largely regulated by the chemistry of the preparation administered. Some extracts stimulate glands, tissues and cells to greater activity, and the resultant mobilization in the blood of defensive elements against cancer. Other extracts tend to slow down glands that have been futile in their efforts to supply defensive elements, because they have been excessively active. Insulin, for example, which is known to slow down the thyroid gland, has been used by experimentalists and also by clinicians, in human cancer. Its action in a number of diseases clearly shows how iodine retention and conservation for effective function has been accomplished.

At this point it may be well to emphasize certain facts that have been brought out by experimentalists and clinicians.

1. Every one of the glands of internal secretion is likely to become cancerous itself.
2. There is no single endocrine gland which cannot be shown to be in some way affected by or related to the development of cancer.
3. All of the glands of internal secretion have yielded extracts which investigators report to be valuable in cancer.

We shall consider each of these points.

CANCER IN ENDOCRINE GLANDS

Thyroid cancers develop commonly from adenomatous goiters. And thyroid cancers send off metastases to the lungs, breasts, brain, lymph-nodes, ovaries, liver and other soft tissues of the abdominal region.

The fact that metastases are so widely spread justifies the evidence gathered by Stocks, Mitchell Stevens, McClendon, and others, including this writer, that cancer is definitely linked with goiter in its distribution. Wegelin has reported that thyroid malignancies numbered 159 in 15,520 necroscopies in Berne, Switzerland, while there were only 13 identifiable as thyroid cancers out of 13,426 necroscopies in Berlin.

Goiter, definitely associated with the development of thyroid cancer, is also known to precede abnormal functioning of the male breasts, and the ultimate development in some men of breast cancers.

Parathyroid tumors are related to excessive losses of calcium, and autopsies disclose their presence in cases of rickets, osteomalacia, and osteitis, all involving calcium losses. Most of the cases are in adults. Calcium and phosphorus metabolism are disturbed, and the bones fracture easily. Cysts in the bones and giant cell bone tumors occur in some cases. The teeth are decalcified.

Adrenal cortex, the outer portion of the suprarenal gland, may become tumorous, and cause profound disturbance of the sex function with apparent masculinity, in adult women. Such tumors have been found in cases of premature sex development in children. Tumors of the internal or *medullary* portion of the adrenals are associated with thyroid overactivity, a diabetic condition, and serious alterations in the blood pressure.

Pituitary tumors, especially those in the anterior portion, cause disturbances of growth. Acromegaly, or gigantism, is due to tumor of the anterior lobe of the pituitary gland.

The commonest tumor of the *thymus* gland is the lymphosarcoma. There may also be metastases from the primary thymus sarcoma. Tumors of the thymus are associated frequently with enlargement of other structures, such as the tonsils and lymphatic glands. Enlargement of the thymus, not tumorous, has been associated with the so-

called "thymus death," and supposed to cause suffocation by pressure on the respiratory apparatus. In adults, thymus tumors are liable to be malignant.

Pineal gland tumors are associated with premature ossification of the bones and premature mental and physical development. The pineal type of sexual prematurity is reported to be commoner in males.

Tumors of the ductless glands are not as a rule developed before puberty. And in the case of the thyroid gland, ordinary goiters may not alter into toxic forms until late in life, as in menopause in women.

The glands of internal secretion *with ducts*, including the reproductive organs, the liver, and the pancreas, are all well known for their capacity to develop cancer. We shall not discuss them separately, but proceed to the interrelationships of glands and cancer.

ENDOCRINE GLANDS AFFECTED BY CANCER

Cramer and Horning, in 1937, pointed out that the whole system of glands of internal secretion was affected in mice when cancer of the breast developed after use of pure "folliculin" to cause such growths.

We know that preliminary abnormal secretion in the male breasts has been reported since the days of Von Basedow as associated with thyroid activity. And cancer of these active breasts may follow. Removal of the prostate gland may be followed by cancer of the male breast, as shown by Petit of Paris. Removal of the male sex glands renders rodents more susceptible to inoculations with transplantable cancer.

Moszkowicz noted that 25% of hermaphrodites are cancerous. And such defects in sex-gland development may be associated with the reports of derangement in the pineal, the adrenal, the pituitary, and the thyroid glands which precede them in many instances.

In rats that had received implants of carcinoma, Guyer learned that the anterior lobe of the pituitary gland had increased numbers of the typical *basophil* cells. From these a potent "sex hormone" was extracted. And we have shown how such a sex hormone may be identified with the presence of iodine in increased amounts, proved by Bennett Allen to be characteristic of pituitary basophile cells after

experimentation. Iodine increase in the anterior pituitary gland follows thyroid feeding, or castration also.

It is not difficult to see how cancer implants, or cancers that arise after irritation and disturbance in the circulation of some region, may cause extremely active glandular function. For these glands are defense organs and control the distribution of essential elements.

Elsewhere, we have brought out the fact that a *cancer* and a *baby* act like parasites, for they need nutritive materials for growth. By their continual demands, they cause all body processes to be speeded up in their "hosts." Exceptionally large amounts of iodine appear, as we know from analyses, in the blood and urine of pregnant women. And Fowweather, in 1930, gave us evidence that a very high iodine content appears in the blood of women in the earlier stages of cancer. In those patients where cancers were advanced, and ulcerous, there was less blood iodine. This is not difficult to explain, since diseased tissues absorb iodine.

The *test for cancer*, described on page 21, in which *abortion* in pregnant rabbits is produced by the injection of urine from cancer patients, may be readily compared to the excessive amounts of iodine released under emotional strain, which we have linked with abortions, due to fright. Miscarriages occur most readily in women during the days in their lunar cycle when menstruation ordinarily appeared. Then it is that the body is known to exhibit high urinary and blood iodine. Iodine stimulates muscle contraction and has been used in Russia to cause abortions.

The "sex hormone" action of the urine of pregnant women when injected into virgin female rabbits can likewise be attributed to the effect of excessive iodine causing ovarian maturity. Sex hormones have been discovered in bile, testes, feces, milk, yeast, coal, various plants, bird's eggs, and the blood of newborn mammals. They are directly active on the reproductive organs, through the iodine present in natural sources. In those synthetic substances which have been *desaturated of iodine*, they cause bodily storehouses of iodine to liberate it into the blood and other body fluids. (Cf. Chidester, *Medical Record*, 1934.)

Some sex hormones, then, are *rich in iodine*, in natural combination with proteins, fats and lipoids, while others are *highly desaturated* in the process of preparation. It is the purest of these latter prepara-

tions that prove to be cancer-forming, just as in the case of shale oil derivatives. For highly unsaturated preparations from the glands, in which the chlorine, bromine and iodine are absent, will initiate, by their demand for iodine, an unusual overactivity of the iodine reservoirs. Following such hyperactivity, there results premature exhaustion of the glands controlling iodine in the body fluids. Experiments have shown that cholesterol is prevented from collecting in blood vessels if iodine is given simultaneously with the fed cholesterol. Moreover, thyroid activity and adequate bodily iodine are known to regulate the proper dispersal of cholesterol.

Theelin, an unsaturated hydrocarbon, now used as a "female sex hormone," is known to cause experimental breast cancer in both male and female mice. A fact which is not appreciated by many doctors is that it has proved valuable, and apparently *safe* in human cases, *when used in combination with thyroid extract or iodine*. The American Medical Association has warned physicians and the public about the dangers of the synthetic "female sex hormones." There have been some reports of tumors following their use.

In the demonstration by Sümegi that cancerous rats are extremely sensitive to adrenal extract, just as in the classic test of Goettsch for *thyroid overactivity*, our argument is strongly supported. Ineffective against cholesterol accumulations, without adequate iodine, the glands may attempt to mobilize it, and thus in cancer their defensive activity causes the signs of hyperthyroidism to appear. Administration of iodine, or of glandular extracts that furnish it, will correct functions and aid in breaking down the cholesterol that feeds the cancer. It is important to note that, as we showed in 1934, iodine is the chemical constituent of value found in all glands of internal secretion (page 200).

Block and Sobotta have recently learned that very high *urinary cholesterol* appears in cancer cases. They attribute this to the breakdown in cholesterol from disintegrating cancers. As we have shown, evidence indicates that high cholesterol is characteristic of the most malignant cancers (page 109). We maintain that increased cholesterol in the blood and urine may be merely an indication that glandular overactivity is withdrawing cholesterol from temporary deposits. Evidence is conclusive that iodine cannot successfully cope with heavy accumulations of cholesterol in cancers, or even in the brain, in cer-

tain types of insanity, unless it is able to reach them. Activated iodine aids in the breakdown of such cholesterol masses. Thus we subscribe to the method of Keegan, in which he used the irradiated blood of pregnant women in human cancer. For pregnancy blood is very high in iodine. (See Sera, page 151; and Irradiated blood, page 138.)

At the June, 1940 session of the American Medical Association in New York, two investigators reported that ultra-violet irradiation conferred on the blood increased effectiveness in destroying bacteria. Such irradiated blood would cause increased activity of the glandular storehouses of iodine, and in the body the combination of iodine trichloride, which Von Behring proved so remarkable in destroying bacteria, and their lipoid coverings.

The writer has, in medical journals, pointed out the fact that thyroid overactivity precedes glandular exhaustion which permits cholesterol to form in gallstones, cataracts, arteriosclerosis, and cancers. In 1930, Koch of Detroit emphasized evidence that in 50% of his own cancer cases there had been a history of previous thyroid overactivity. Shirlaw, of Wigan, England, found that previous histories of excessively high urinary and blood sugar existed in many of his patients who later developed cancer. Thyroid overactivity is associated with diabetic conditions, as we have reported previously (1934).

Wilder of the Mayo Clinic and Ryan of the Cleveland Clinic have recently discussed hyperthyroidism in diabetics. We found diabetes to be associated with hyperthyroidism and resultant heavy calcium losses in incipient rickets, also. (*Int. Clin.*, 1934.)

EXPERIMENTAL AND CLINICAL USE OF GLANDULAR THERAPY IN CANCER

"God,—through time and experience works out many hidden truths; to suppress these would be no other than injurious to mankind, whose minds, like unto so many candles, should be kindled by each other."

—BISHOP HALL

As we shall attempt to show, the glandular therapy that is most effective in experimental cancer, and in human cases, is designed to normalize the deranged metabolism, and to insure adequate amounts

of protective elements. It will become increasingly apparent that other means of treatment of cancer, recognized as valuable, may very well prove to exert their influence by the direct or indirect stimulation which causes the use of released protective agents. It may thus actually alter local conditions that favor excessive or abnormal growth.

When a small piece of a tumor is removed for pathological study (biopsy), it has been noted that some tumors regress without further treatment. Likewise, experimentalists, thrilled with the evidence that foreign proteins, or various chemicals, injected into growing cancers will cause them to become smaller, have been confounded by the fact that ordinary distilled water injections may produce similar effects.

These facts merely indicate the delicate balance existing in the chemistry of growing cancers. For *chlorides*, or *iodides*, are known to induce regressions also. And the addition of highly unsaturated fatty acids (as in tethelin studies, page 176) will cause tumors to grow more rapidly just as tissue cultures do.

The striking results obtained by experimentalists and also by clinicians, using glandular extracts, are not lightly to be cast aside. They are based on the unquestioned influence of glandular extracts on cell and tissue growth. Failure to influence cancers by some workers with extracts can be blamed on faulty supportive diet, and in many cases on a contemptuous attitude which prevents a scientific trial. The thoroughly prejudiced as well as ignorant person will sometimes dismiss, after trials with three, two, or even *one* mouse, the results obtained by careful students with hundreds of animals and numerous human cases. Such instances of ineptness are actually on record in the literature.

No reasonable attack on cancer should be dismissed. Certainly the use of glandular extracts and of supportive medication seems preferable to defeatism, and the overweening prejudice of some cancer experts whose patients all die. Cancer patients are entitled to the same attention to their anemic and run-down states that others receive.

Thyroid Gland

In 1896, Robert Bell reported that thyroid extract was far superior to extracts from the parotid (a salivary gland), and the mam-

mary glands in human cancer. He cited recoveries persistent as long as 9 years. His strict attention to the relief of intestinal obstructions, and advocacy of a diet rich in fresh fruits and vegetables, undoubtedly contributed to the cures. Four of his cases have been widely discussed by advocates of dietary adjuncts to cancer control, for they represented supposedly "incurable" cancers.

Bishop, in 1898, and Beaver, in 1902, also were early users of thyroid extract in doses up to 15 grains a day, reporting cancer regressions.

Boyd, in 1900, and Butlin, in 1902, were among the earliest clinicians to emphasize the value of *thyroid extract* after removal of the ovaries in cases of cancer of the breast. Boyd warned of the fatal nephritis that may follow heavy thyroid dosage after glandular disturbance caused by the cancers.

Ovariectomy and its influence on the excessive losses of calcium in pregnancy (osteomalacia) have been known for about 50 years. The use of ovariectomy, and of accompanying thyroid therapy, in cancer of the breast, was an outgrowth of the special knowledge of Blair Bell. Bell emphasized the rôle of the *thyroid gland* in conserving *calcium*; and he described the effectiveness of *ovariectomy* in curing osteomalacia of pregnancy. Veterinarians have for many years had a tradition regarding the effect of spaying female dogs which had mammary cancers. Our earliest research work on ovariectomy and the prevention of breast cancers in mice was that of Leo Loeb (page 191).

Mixed glandular preparations, including thyroid, adrenal and pituitary extracts, were used by Shirlaw successfully in 1913. Shirlaw informed the writer of his use of liver extract in cancer in 1936.

Naame considered thyroid extract to be indispensable in the treatment of cancer. He stated that the glandular secretions in normal function insure the harmony and proper equilibrium between cell dissolution and cell growth. The altered functioning of the endocrine glands leads to the formation of atypical or cancer cells.

Naame cured 2 cases of carcinoma with thyroid-mammary gland extracts. Other cases of facial cancer were cured in elderly women by similar treatment. (*Gazette des Hopiteaux*, Paris, 1921.) Naame has more recently used combinations of thyroid, adrenal, and liver extracts with success in human cancers.

Experiments with animals include those of Matsuoka, who removed the thyroid gland in rabbits and noted growth acceleration of their cancers. Implants of thyroid gland, or injected potassium iodide, caused retardation in growth of tumors, and decreased the migration of metastases.

Gilroy, in 1930, prevented the growth of tumors in 165 mice by injections of thyroxin (65% iodine). Other studies, including those of Meyer and Aub in 1933, indicate the rôle of thyroxin in slowing the growth of mouse cancers.

Iodine, in sufficient or in excessive amounts, has been shown by Sugiura and Benedict, 1935, to induce a high percentage of "takes," and slow regression in experimental mouse cancers. But a normal amount of iodine, such as others had shown would protect against goiter in experimental animals, induced regressions of experimental cancers and prevented successful implantations.

Colloidal iodine has been used with success by a distinguished clinician since 1925, and he reports cures up to 12 years standing in certain types of cancers. His amazing record in the cure of rectal cancer cannot be given in its entirety until it is published by him. Like so many able clinicians, he does not publicize his findings, but his work is well known in his group of friends.

Eppinger, in 1931, and Cohen, in 1935, have used thyroid extract with marked success in cutaneous ulcers.

When Brown and Pearce, in 1923, showed that the activity of the thyroid, adrenals and reproductive organs in experimental rats indicated their degree of resistance to cancer implants, they gave us valuable evidence. For these same workers also showed how glandular function was involved in the resistance of rabbits to attempted infection with syphilis. Iodine is recognized as a specific in syphilis.

Parathyroid Glands

The very high concentration of iodine in the parathyroids which Gley reported in 1897 would seem to follow from their location as masses of fatlike cells imbedded in the thyroid gland. As early as 1927, McCann found that parathyroid extract plus added calcium benefited human cancer. Reding and Slosse were able in 8 days to raise the blood calcium with parathyroid extract, in a woman who had

previously been operated on for mammary cancer. They were not treating the cancer of course.

Koch, of Detroit, reported in 1930 the successful use of parathyroid extract in inoperable cancers. He found that the glands of internal secretion which are most commonly deranged in cancer patients are the parathyroids, thyroid, prostate, pancreas and adrenals. Previous profound overactivity of the thyroid gland was the history of 50% of the cases of cancer that came to his notice. And such derangement would be associated with abnormalities in the other glands of internal secretion. Castration involves changes in the iodine content of the other endosecretory glands.

Beale and other clinicians of the writer's correspondence have used parathyroid extract, and calcium as lime water, calcium gluconate, or calcium lactate, in human cancers.

J. H. Thompson, using daily injections (subcutaneously) of extracts from the *parathyroid glands*, secured encouraging results with hopeless cases of human cancer. The discovery was made at the charity-run Hosa Laboratories. There were 30 assistants, and 1200 physicians collaborated in trials at 200 hospitals. The announcement was made by Sir George Gibson Mitcheson, M.P., who founded the Hosa Laboratories. According to *Time* (April 3, 1944) the British Medical Research Union was optimistic. The usual expressions of doubt, and even dismissal as of no value, were cited on inquiry from some cancer experts in the United States.

Thymus

The thymus gland, located in the region just behind the isthmus connecting the thyroid lobes, and anterior to the heart, seems to be linked closely with the activity of the thyroid and the reproductive organs. In goitrous regions, the thymus may be persistently enlarged, after puberty, when it ordinarily regresses. It is also exceptionally large and "persistent" after puberty, in individuals with reproductive gland insufficiency, or in cases where animals have been castrated.

Experimentally, Rowntree has shown that thymus extract furnishes growth substance, identified as amino-acids, which cause mice and rats to grow exceptionally large, reaching adult size rapidly, and

to mature early. After several generations from stock in which pregnant females were injected with extracts from thymus supplied by Hanson, the rodents surpass the control animals in an astounding manner. The thymus extracts in Rowntree's tests have come from the laboratory of Dr. A. Hanson, of Faribault, Minnesota.

Hanson, in 1930, reported on clinical experience in which 4 cases of inoperable human cancer benefited by intramuscular injections of calves' thymus. Maeda, in the same year, reported similar regressions for cancers in the rabbit given thymus extracts.

Since his first success with thymus extract, Hanson has secured the cooperation of a medical group who have tested his extract (prepared from the thymus of calves under six weeks of age) with more than a hundred cases, some of which were benefited. Hanson's best results were obtained with visceral adeno-carcinoma. He writes a supplemental note for this section, to the effect that his extract retards certain types of carcinomas, but that it apparently *stimulates* the *growth* of some *sarcomas*. Hanson was first to develop an effective *parathyroid extract* for use in parathyroid tetany, and is so credited (1924).

Karnicki, in 1932, used injections of thymus extract, and also implants of the gland, with success in experimental cancer in rabbits. Maisin, in 1935, used thymus extracts to inhibit growth of tar cancers.

In 1908, Gwyer (*Ann. Surg.*, 47, 506) reported clinical findings that indicated the value of dried thymus gland in cases of inoperable human cancer. M. Murray (*J. Lab. and Clin. Med.*, 24, 1247, 1939) found that in rats that were most resistant to transplants of a breast carcinoma the thymus gland was persistently large. Tests showed that previously implanted *rat thymus* inhibited the growth of the transplants of cancer in rats.

Opposing these findings we have the reports of Meyer, 1931, and of Simpson, 1931. Meyer and Simmons, using Hanson's technique, secured no evidence of regression in a mouse carcinoma. Simpson and Marsh, with three albino mice afflicted with a spontaneous adeno-carcinoma of the breast, were unable to secure any benefit by a thymus extract.

Scathing reviews of reports by pioneers of successful treatment of large numbers of animals and human cases have frequently been

made on the basis of a few inadequate experiments. This was seen in the case of Ishihara and his POU hormone. (See page 189.)

Suprenals

In 1929, Sokoloff reported the successful use of a combination of dialyzed extracts of the suprarenal gland, combined with iron, which he called "corferrol." He treated 600 mice, and reported a high percentage of regression of implanted tumors. Critics of his work did not deny the fact that unbiased observers had noted regressions, but the work has not received much attention. Later Sokoloff and Taylor, in 1931, gave the results of similar experiments with rat and mouse sarcomas, in which they cured 80% of the group of 300 animals.

An example of the type of review made is that of the critics who cited identical results obtained with zinc chloride and adrenalin chloride. It would seem possible that chlorides could prove valuable in experimental cancer, since zinc chloride has been used for centuries in human cancer as an escharotic. It is the basis for several "secret" methods by unlicensed persons.

In 1930, Coffey and Humber first reported their successful use of an adrenal preparation in human cases. They were swamped with requests from frantic cancer victims, and have treated "hopeless" cases.

The Kellogg Foundation in Los Angeles gave an opportunity for treatment by the Coffey-Humber extract (which is patented), and in 1931 Dr. R. H. Harris gave a report on results with 415 cases of sarcoma and carcinoma.

With advanced and incurable cases treated, the suprarenal cortex extract was effective in improving the appetite and general well being of many, but in no case proved curative. As in so many treatments, the sloughing away and necrosis of the cancers was followed by evidence of toxic effects. Supervised *supportive medication* was lacking, for the Coffey-Humber extracts were the only contribution of that group to the cases otherwise handled by the Kellogg Foundation.

In 1938, Coffey and Humber reported to the American College of Surgeons on the complete cure of 53 supposedly hopeless cases of cancer, deemed inoperable, which after their treatment had lasted 5

years or longer. Prejudice is increased because their extract is *patented*.

Sugiura and Benedict, in 1930, were able to prevent the development and growth of small malignant tumors in rodents by intratumoral injections of suprarenalin, but they failed with distant injections. They attributed the favorable results to the vaso-constrictive effects of suprarenalin, which are also possessed by extracts from other glands.

Arloing and associates of Paris found, in 1933, that injections of a protein precipitate extracted from calf suprarenals greatly inhibited the growth of mouse tumors.

Bischoff, Maxwell and Ullman, of California, have tested the Sokoloff and the Coffey-Humber types of adrenal extracts, with mice, and found that tumor growth was little affected by them.

In no case of experimental use of adrenal (suprarenal) extracts has there been any apparent realization of the significance of supportive treatment, with diet, and supplemental calcium, iron, iodine, and fats. This is necessary in all attacks on a disease where heavy losses of minerals and body-building nutriments have occurred. (See page 50.)

In the tests with thymus and adrenal cortex extract made by Hruhzt (1930) the preparations were made by saturating the adrenal cortex with NaCl and then discarding the filtrate. Such a method would (as every druggist knows) cause the extraction from the gland of iodine, which passed into the filtrate. It is of little import that the extracts were ineffective on experimental carcinoma and sarcoma of albino rats. (See Hruhzt, C. M., *Ann. Int. Med.*, 1930-1931, 4, 1589-1597.)

Increased interest in the relationship between the adrenals (suprarenals) and cancer has been manifested since these glands have been considered in relation to the susceptibility of rats to transplanted lymphatic leukemia. At Memorial Hospital, Dobriner and Rhoads, and at Harvard University, Lieberman, Hill and Fieser (1944) have furnished evidence that leukemia (called blood cancer) may develop because of disturbed function of the adrenal glands. And J. B. Murphy (Rockefeller Institute) has shown that in adrenalectomized rats there is greatly increased susceptibility to leukemia transplants.

Murphy has also found (*Science*, April 14, 1944, vol. 99, p. 303) that both the adrenal cortex hormone and the pituitary adrenotropic hormone furnish protection against the successful inoculation of rats (intraperitoneally) with this transplantable disease. No clinical evidence of human treatment, or even of cases of spontaneous leukemia in animals, has been furnished as yet by the workers named, and Murphy warns us against unjustifiable optimism.

Pituitary Gland

Early work with extracts from the anterior pituitary gland by Robertson, in 1916, showed that his "tethelin" caused greatly accelerated growth of inoculated tumors in rats. Erdmann, in 1918, reported that Robertson's "tethelin" caused a three-fold increase in the growth of subcutaneously implanted cysts in the fowl.

Ewe, in 1919, by adding iodine to tethelin, caused it to lose its growth-promoting power. Our explanation of the reason for this action of iodine is based on the fact that tethelin, which consists of unsaturated fatty acids and lipoids (Robertson, Drummond and Cannan), was able to stimulate growth in tumors, by offsetting and balancing the iodine in them. Added iodine would again cause regression.

It is interesting to note that Bischoff, Maxwell and Ullman, in 1931; Gross, in 1933; and Wiesner, also in 1933, have reported that their special extracts from the anterior pituitary gland caused increased growth in tumors of rats and mice. Multiple *transplants* of the anterior lobe cause cancer of the breast.

Due probably to different methods of preparation, and resultant differences in chemical composition, we have the experimental findings of Zondek, in 1932; and of Reiss, in 1933, who were able to prevent the growth and even to induce regression of mouse tumors by anterior lobe extracts. *Chlorine*, from the HCl or NaCl used in processing, or *iodine* normally found in high concentrations in the anterior lobe of the pituitary gland, could aid in cancer control, by such extracts. (See Chlorine, page 132, and Iodine, page 136.)

One of the most significant reports of the protective antagonistic action of a glandular extract against the cancer-inducing properties of a synthetic substance lacking iodine is that of Cramer and Horning,

in 1938. These investigators had been struck by the fact that after *theelin* (also called *folliculin*), the "female sex hormone," has been injected into rodents for a time, breast cancer results.

Theelin causes great overactivity of the anterior pituitary, thyroid, suprarenals, pancreas, sexual glands, and breasts. Even in castrated males, the enlarged mammary glands secrete milk. This feverish activity is followed by premature exhaustion of the whole endocrine system, with degeneration and atrophy. Cramer fortunately selected the *thyreotropic hormone* of the pituitary gland in the hope that its extract would prevent glandular injury, after *theelin*.

In many cases, the abnormally engorged breasts, clogged with accumulations of unsaturated sterols, unsaturated acids, and other growth-promoting substances, develop lumps. Atrophy of the protective endocrines prevents the proper distribution of elements that are capable of dispersing the masses, and breast cancers develop. In women, tumors of the breasts and uterus have been recorded after continued dosage with *theelin*.

Not only do the estrogenic hormones produce cancer in animals when *injected*, but certain of them if applied to the *skin* of the *back* in mice produce a profound systemic reaction, and cancer of the breast results.

Disturbance of the sex cycle in experimental animals has long been known to cause the development of breast cancers. (See pages 123, 225.) Cramer and Horning found that only the *purest* preparations of "folliculin" (the female sex hormone) caused mammary cancer.

This indicates to the writer a condition of *unsaturation* that is comparable to cancer production by the *unsaturated hydrocarbons* found in shale oils. In these highly refined substances, those with the "highest iodine numbers" were the most effective in producing experimental cancers. (See page 207.) The "sex hormones" are unsaturated hydrocarbons, related to the sterols.

There is great variation in the clinical and experimental findings after hormone therapy because extracts are prepared by so many different methods. Some, resembling the natural substance, retain the lipoids, fats and minerals; others are defatted, or demineralized, or both. The synthetic substitutes for glands are the most potent and, of course, the most dangerous.

The early "sex hormones" were extracts from the ovaries of sheep and pigs, and varied in potency and chemical composition. Much of their value was due to the fact that lipoids and fats and the *iodine* were all retained in these well-balanced extracts.

Female sex hormones have been obtained from the placenta of women and of animals; they have also been prepared from the thyroid gland, the pituitary gland, from fish sperms, and from the testes of the bull and the horse. Coal, petroleum and various plants are also sources.

The female sex hormones in use today, called "folliculin," "menformon," or "theelin," are crystalline, *desaturated* substances derived from the urine of animals. It is a bizarre fact that the richest source of the *female sex hormone* is the urine of the *stallion*.

Theelin is "an *unsaturated* keto-monatomic alcohol, with an iodine number of 86.7," and like shale oil hydrocarbons is most potent in cancer formation when it is in the *purest* state. Thus we would naturally expect that by its *demand* for iodine it would set up great overactivity of the iodine-rich glands.

Theelin shares with a number of substances the ability to produce cancer following a period of extremely marked stimulating action on the glands of internal secretion, including the ovaries and testes. Chemically, these substances, including hydrocarbons and sterols, resemble each other in several ways including their *unsaturated nature*. We shall discuss "Unsaturated substances" elsewhere. (See page 207.)

In using such a powerful stimulator of the female reproductive system as *theelin* in human cases there is risk, for tumors of the breasts and uterus have been recorded after continued injections of theelin in women. The body's resistance to high doses is centered in the *liver* for the most part.

Theelin is used with some degree of safety in combination with thyroid extract, or iodine. (See page 167.) The guarding effect of iodine is important in this as well as other cases of "unsaturated" substances that cause overactivity and early exhaustion of the glands of internal secretion. (See page 207, Unsaturated substances and cancer.)

Thyroid extract and iodine stimulate the glands of internal secre-

tion and cause them to become active. But both thyroid extract and iodine are furnishing needed iodine, and merely hastening normal processes, without robbing the body of minerals. True, heavy thyroid or iodine dosage will cause the rapid loss of fats and lipoids, and in excess they may even rob the nerves of their protective myelin. (See Vitamin B, page 81.)

It is well known that milk secretion in cattle is increased by feeding *thyroid extract* or *iodine*. And in the experiments of Steinach, in 1912, he learned that transplants and injections of extracts from the ovaries of rabbits would cause milk secretion in the breasts of young castrated and normal male rabbits.

The disease known as *gynecomastia*, in which the *human* male breasts become enlarged and even secrete milk, has long been known as a precursor of *cancer of the breasts*. There is a clinical link between gynecomastia and the thyroid gland. Since the early studies of Von Basedow, in 1848, physicians have reported that hyperthyroidism in men was sometimes followed by such abnormal breast function. In 1935, Starr described two such cases of overactive thyroids followed by gynecomastia, and he gave an extensive literature survey showing similar cases.

Castrated or eunuchoid men are notably subject to breast cancer. Great increase in the *iodine* content of the thyroid gland has been noted in gelded horses and ovariectomized rats. Subsequent glandular exhaustion may permit cancer growth.

Theelin, by its demand for iodine, causes extreme *hyperthyroid activity*, and thus *castration* paves the way for early exhaustion of the whole endocrine system, all the glands of which are iodine reservoirs. (See page 200.)

Theelin causes the same change from male to heavy plumage in castrated male birds that has likewise been recorded with thyroid extract by many experimentalists. Thyroid extract is *rich in iodine*.

Theelin, by its very *unsaturated* nature, is able to demand iodine, and to cause the iodine-rich glands to become active in order to supply the iodine needed. Such hyperfunction results in a general glandular upset, and eventually the body loses its power to cope with accumulated debris. The well-known fact that iodine in normal amounts will prevent accumulations of *cholesterol* and other lipoids

and unsaturated substances common in cancer brings us to the logical fact that iodine is necessary in the body to ward off cancer and other cholesterol-induced diseases.

Iodine and thyroid extract produce thyroid overactivity and affect the function and the iodine content of other glands of internal secretion. In proper dosages, iodine is extremely effective in normalizing glands. But the "unsaturated" substances, including *theelin*, unsaturated fatty acids, and iodine-lacking carbohydrates, and amino-acids, will also cause thyroid overactivity. They do this by *demanding iodine*, and they cannot stabilize the glands through fats, lipoids and balancing iodine in themselves, as do natural gland extracts. (See Fat-thyroid-iodine balance of McCarrison, page 65.) *Unsaturated hydrocarbons* are well known in experimental cancer (page 216).

The thyreotropic hormone of the anterior pituitary is important in mobilizing iodine to offset the unsaturated "theelin" and thus in controlling and preventing *thyroid overactivity*, and it acts as does pure thyroid extract to cause an increase in the size and number of islets in the pancreas. Thus Cramer was unwittingly influencing the simultaneous combustion of *fats* and *carbohydrates* that Shirlaw has pointed out (page 183) is so significant in preventing an abnormal metabolism that favors cancer.

Our interpretation of Cramer's protective "thyreotropic" extract of the anterior pituitary is that it stabilizes function in the thyroid-pituitary-ovary complex, preserves the iodine needed for effective control of the unsaturated acids and lipoids, and thus insures iodine essential for normal sex cycle, and the normally rapid circulation of lipoids, proteins, fats, carbohydrates and minerals through the mammary glands as well as the rest of the body. By preventing the speedy exhaustion of the glands of internal secretion, ordinarily induced by the chemical demands of *theelin*, the thyreotropic hormone keeps metabolism normal.

Liver

Liver extracts have been little used in experimental cancer, but the value of liver as a source of the vitamins has led to recognition of its possible use as an adjunct to other treatments in human cancer.

Byla, in 1913, cited the early use of liver juice in human cancer.

By direct treatment, Von Leyden was able to bring about liquefaction of cancers. He assumed that liver extract furnished certain ferments that broke down proteins.

In a letter to the author, dated May 5, 1934, Doctor J. Thomson Shirlaw stated, "I feel sure that you are on the right lines; I like your theory of the regulation of calcium, iodine, sugar, and fats; the liver plays an important part." Dr. Shirlaw then cited the case of a lady of 70 years, with cancer of the pyloric region of the stomach and of the duodenum, to whom he gave massive doses of liver extract. She made a remarkable recovery and died from another disease at the age of 82.

In using a commercial preparation of "liver lipase" by the intravenous route, Dr. Shirlaw was unable to cure rectal carcinoma. National clinical correspondence-groups with whom the writer began working in 1933, have found that *some* commercial gland extracts were quite inert. Several clinical groups have prepared their own complete extracts, which were highly potent and apparently safe. Dr. F. Vásárhelyi, formerly associated with Hans Januschek in Vienna, is now in New York City, associated with Dr. S. G. Frank in the preparation and use of *natural hormone extracts* from freshly slaughtered animals. They administer these in various diseases in combination with fresh vegetable juices furnishing vitamins and minerals.

Since iodine is present in all the endocrine glands, and guards against possible injury such as is produced by the unsaturated hydrocarbons in synthetic "sex hormones," it has been for ten years our recommendation that theelin and similar carcinogenic "female sex hormones" be accompanied by thyroid extract or iodine.

Liver extract and cod liver oils normally contain large amounts of iodine, thus being more beneficial and safer than the strange combinations which include excessive (added) Vitamin D.

Liver extract has been used by Douglas-Webster of London, and by Anderson in the form of intramuscular injections, to improve the condition of patients suffering from radiant energy sickness. *Iron*, in addition to liver extract, is valuable, according to Anderson.

As discussed previously (page —), this writer subscribes most heartily to a combination of liver extract and iron, in radiant energy

sickness. For in 1928, without realizing the importance of the discovery, we were able to offset to some extent the injurious effects of Vitamin D (the "sunshine vitamin") in rats by iron and iodine in extremely minute doses. In 1930, Dr. Howard Eder, of California, published his remarkable report on the benefits derived by children and even adults, who had been too much exposed to the sun, after they had received his preparation of cod liver oil plus ferrous carbonate. He did not then know the high iodine content of the best cod liver oils (which this writer has long stressed to his clinical groups) and he had not seen the 1922 report of Quimby on the value of iodine for X-ray workers who had been themselves radiated. Throughout a lively correspondence of 7 years, Doctor Eder and the writer have concurred on the great value of minerals in disease.

Dr. D. T. Quigley, a radiologist and surgeon, is one of the alert clinicians who uses supportive medicinal and dietary treatments in cancer. We find ourselves in complete agreement on minerals and vitamins. His success in anemias, heart disease and cancer with *multiple* vitamin and mineral therapy has been recorded elsewhere. He is careful to include calcium, iodine and iron in the diet, or as medication. These are the elements which this writer has emphasized in medical journal articles on vitamins, minerals, glands, and cancer during the past 15 years. It is necessary to restore these elements in cancer as in anemias, and with pregnant women.

Liver extract is remarkable for its ability to aid in normalizing the glands of internal secretion in vitamin deficiencies. It is a rich source of calcium and of iodine. Liver contains iron (large amounts in the rabbit), but has less iron than the spleen. The technique adopted by Douglas-Webster and by Anderson in cases of radiant energy sickness, and by Eder in sun injury, seems just the proper one.

Clinicians with whom this writer has been in touch since 1933, in his capacity as Consultant in Endocrinology, have reported successful use of liver extract in human cancer as an adjunct to other treatment. Our emphasis on the necessity for replacing iron-iodine-calcium losses has been productive of excellent clinical results. And, after all, these are the important ones.

Pancreas

J. T. Shirlaw, of Wigan, England, reported in 1929 on the relationship between early evidence of high blood and urinary sugar, in his cases, and the later development of cancer. His theory is that cancer develops in cells that have been *exhausted of fats*, which reduces their cohesive power, and permits irregular cell union and cell multiplication. His emphasis on the need for simultaneously burning *fats* and *carbohydrates* is in line with our own conception. Nevertheless, we hold that calcium retention in adequate amounts, under normal glandular conditions, will prevent wild cell dispersal. Thyroid extract stimulates adequate fat formation, Shirlaw believes. We attribute lack of cohesion and rapid cell division to losses of needed calcium, which is controlled by the glands of internal secretion.

Langston found in 1922 that the *blood sugar* test in cancer is much like that in heightened activity of the thyroid. Hyperthyroidism is seen in diabetics.

Cramer and associates, in 1926, found that *insulin* is present in normal tissues in appreciable amounts, but is absent from malignant cancers. The cells of normal tissues oxidize glucose, while the cells of cancers split glucose with the formation of excessive amounts of lactic acid, as shown by Warburg. In his tests, Warburg showed that tumor tissue removed from 50% to 70% of the glucose from circulating blood in rats.

Pautrier, in 1926, recorded successful use of insulin with leg ulcers. And Meyer, in 1933, found that insulin decreased the speed of glycolysis, in which glycogen was broken down into lactic acid, in mouse sarcoma.

Kawamura, in 1930, was able to prevent growth of tar tumors with insulin. Lambret, in 1933, caused regression of rat sarcomas in 70% of cases by injecting insulin subcutaneously at a distance from the tumors.

Beginning with the treatment of certain circulatory disturbances by insulin, Beale of Massachusetts has used insulin in a variety of diseases including cancer. His method in cancer includes the use of small doses (3 units) of insulin plus parathyroid extract, and liver extracts with supportive calcium. The diet is rich in vitamins and

minerals. Other physicians in a number of states, to whom this writer was able to bring news of Beale's success, have concurred with him on the value of his treatment. Beale believes that insulin thus supported is valuable as an adjunct to the recognized attacks by surgery and radiant energy. At a meeting of one of the medical societies, this writer had an opportunity to talk with clinicians who had been successful by Beale's method. It is unfortunate that, as in so many instances, patients cannot have the advantage of supportive treatment even before their operations. Postoperative *embolisms* have been practically eliminated at some great clinics by proper iodine medication, before the various operations.

Tissue lipolysis is defective in cancer, according to Shaw-Mackenzie. That is, he has noted that ability to break down fatty substances is not normal. Since insulin favors the coincidental destruction of fats and carbohydrates, he favors its use in cancer. (See page 31.)

Burstenbinder, in 1932, stated, "The cancer patient is a diabetic, and sugar is conserved by the cancer cells." (See page 60, Carbohydrates.)

The fact that cataracts, gallstones, and certain abnormal mental states which involve cholesterol accumulations are benefitted by insulin gives support to the conclusion that iodine retention and use are effected by insulin. Moreover, Lepine, Lawrence, and Hendry independently recorded the successful use of insulin in *hyperthyroidism*.

This writer has published numerous medical journal articles, indicating how the thyroid gland is overactivated in diseases, including diabetes, tuberculosis, and cancer. And he has talked with some clinicians and corresponded with others who know the value of insulin in cancer. The key to control of cancer in some cases is in the retention of defensive elements, now wasted by ineffective, exaggerated efforts of endocrine glands.

In their book, "The Biochemistry of Malignant Tumors," Stern and Willheim (1943) mention the fact that hypertrophic islets of Langerhans in the pancreas of animals or humans with cancer have been viewed by some authors as indications of the defensive reaction of the organism. Experiments with carbohydrates ingested orally or

injected into animals "clearly indicate the tumor producing effect of carbohydrates; consequently substances which cause hypoglycemia may be expected to influence tumor growth in the opposite manner."

Waterman (1925) caused inhibition of inoculated tumors by preceding administration of insulin. Similar results were obtained in the Ehrlich mouse carcinoma (Silberstein, 1925); and in tar carcinoma cancers (V. Witzleben, 1925). We have previously noted the studies of Lambret and Driessens, where insulin injections inhibited the growth of the Jensen rat sarcoma in 70% of animals treated (1933).

Stern and Willheim (page 594 of their book) are evidently not informed regarding the clinical support for Beale's thesis on insulin, but they explain failure in tests with animals run by Dr. Beale and Dr. Shields Warren of Harvard (*Am. J. of Cancer*, 27, 99, 1936) as probably due to the carbohydrate-rich diet furnished with the insulin treatment in animals studied. This excessive carbohydrate intake would oppose the insulin and permit the accumulation of glycogen and the formation of lactic acid, favoring tumor growth.

This writer has published numerous medical journal articles indicating how the thyroid gland is overactivated in diseases, including diabetes, tuberculosis, and cancer. And he has talked with some clinicians and corresponded with others who know the value of insulin in cancer. The key to control of cancer in some cases is in the retention of defensive elements, now wasted by ineffective exaggerated efforts of endocrine glands, excessively functioning. Dietary and medicinal adjuncts are here indicated to aid other therapy.

Studies by Ryer and Murlin (*Am. Soc. for Exp. Pathol.*, 28th Ann. Meeting, Chicago, April 17-19, 1941) included the use of insulin, thyroxin and insulin, and thyroxin alone, in rabbits inoculated with the Brown-Pearce epithelioma. They report marked reduction of metastatic growths as a result of these studies. Later publications should be of great interest.

Testes

One of the earliest reports of the beneficial use of testicular extract is that of Rho, who cured leg ulcers with it. In 1931, Duran-Reynals

of the Rockefeller Institute found that the growth of rodent tumors was retarded when they were added to testicular extract. Normal rabbit serum caused rapid growth of the tumors.

Loeser, using the new synthetic male sex hormone, *testosterone propionate*, reported in 1931 that it relieved pathological conditions in the uterus, and caused the disappearance of lumps in the female breasts. It also cured mastitis and inflammatory conditions of the mammary glands which are sometimes followed by cancer. Other clinicians have used testosterone propionate in the successful treatment of prostatic enlargements.

Dr. Frank E. Adair, chief surgeon at Memorial Hospital, New York, has used *testosterone* in the treatment of advanced cancer in women. While he is most careful to state that in his experience the method is not a cancer cure, he finds that pain is greatly reduced and he considers that the *male sex hormone* behaves in an antagonistic manner, and reduces the activities of the female reproductive organs.

Precancerous changes in the ovaries of rats have been produced by large amounts of testosterone propionate, or of the female sex hormone, estrone. (Shay, Gerson-Cohen, Paschkis and Fels, *Endocrinol.*, 1939, 25, 933 —.)

Injections of testosterone propionate into young virgin female mice prevented the normally high incidence of breast cancers in a cancerous strain. But females that had borne young were not protected (E. Jones, 1941).

Tests with the male sex hormone made with mice that had developed cancer after treatment with the chemical agents *benzpyrene* and *methyl-cholanthrene* showed that large doses of the hormone could only inhibit somewhat the transformation of papillomas into malignant tumors (Flaks of France).

Using the transplanted Brown-Pearce carcinoma, Murlin and associates (Rochester University) found that male sex hormones extracted from urine would check the development of secondary (metastatic) tumors in rabbits. *Testosterone* injections in small doses caused retarded growth of the tumor implants and prevented successful "takes" in some animals. Large doses of the hormone seemed to hasten the metastatic spread of the tumors. The Rochester group found that some pure hormones had no effect on either im-

plants or on secondary growths. They therefore inquire whether some other substance besides the hormone may not be involved in successful tests. (Murlin et alii, *Science*, 90, 275, 1939.)

Huggins and associates (Chicago) have been securing excellent results in prostatic cancer after complete bilateral castration. Of 21 cases of human prostatic carcinoma, 15 were definitely improved. Huggins has also evaluated the androgens (male sex hormones) as stimulating prostatic cancer growth; while his clinical tests show that the female sex hormone (estrogens) will, like castration, reduce the *serum acid phosphatase* and inhibit greatly the growth of the prostatic cancers.

H. L. Kretschmer has reported on eleven cases of prostate cancer from his own service in the Presbyterian Hospital (Chicago), five of whom had bone metastasis. From the case records, he is inclined to believe that insufficient time has elapsed since orchidectomy was instituted to tell about cures by this method. (Kretschmer, *Jour. Amer. Med. Assn.* 123, 755 (Nov. 20), 1943.)

In our own work with clinicians, we have noted the fact that the normal prostate gland is rich in iodine, and that iodine applications in the prostatic region have benefitted cases of prostatitis in the aged. It is also significant to note that after castration Klein discovered an increase in the thyroid iodine of *geldings* up to 55% more than in stallions.

Perhaps the metastatic spread of the Brown-Pearce carcinoma in rabbits described by Murlin's group after heavy doses of *testosterone*, may be explained by Nathanson's discovery (1940). For he found that the *thyroid* and *parathyroid* glands were stimulated in immature female rats after they had received *testosterone propionate*. The thyroid and the parathyroid glands are rich in iodine. In fact the parathyroid glands contain 35 times as much as the thyroid, proportionately (E. Gley). Nathanson implicates the anterior lobe of the pituitary gland also. This gland is a well-known storehouse for iodine, as is the adjacent midbrain.

Hyperactive glands of internal secretion will cause the liberation of large amounts of iodine, calcium and other elements into the body fluids. If excessive amounts of iodine cause tumors to break down too rapidly, the dispersal of metastatic fragments may occur. More-

over, enormous losses of calcium (250% greater) occur in hyperthyroidism.

On the other hand, the moderate release of iodine after small doses of *testosterone propionate* will facilitate the slower disintegration of tumors. With moderate activity of the thyroid and parathyroid glands, calcium becomes available to prevent metastases, and to control cell divisions. We must point out the fact that even slight stimulation of the endocrines will create the need for the small amounts of iodine that the body must have at all times.

Ovaries

Cancer of the ovaries frequently appears as metastases from the thyroid gland. And benign tumors of the thyroid can become malignant after they have been dispersed. Plaut recorded *thyroid tissue* in ovarian tumors and, besides identifying it microscopically, analyzed it for iodine. He also used the classical test, and hastened the metamorphosis of tadpoles into frogs with the tumor substance. In the same year (1933) Masson studied six cases of ovarian tumor in which large amounts of iodine-containing thyroid tissue were found.

The ovaries, when tumorous, will inhibit growths of transplanted tumors, however, as shown by Himeno. Furthermore, there is antagonism between growing embryos and implanted cancers, if they are adjacent to the embryos in mice. This last discovery, by Warner, shows how there is apparently a similar demand for the same food-stuffs; but it also may indicate that the stimulating effects of the embryos and tumors cause the necessary cancer-destroying elements to be mobilized in excess. In any case, the growth processes are inhibited in both cancer and embryos.

Ovarian extracts have been used in cases of prematurely born children, and Nollé found them valuable for tiny 2 or 3 pound infants. But this is an instance where thyroid extract has been long known to be efficacious. Ovarian extracts from pigs' ovaries were used in menopausal difficulties in women for 20 years before the new, sometimes dangerous "female sex hormones" were developed. The ovaries rank next to the thyroid gland in iodine content, according to the studies made by the Lahey Clinic in 1939. Ovarian extract benefits

goiter, but the new *folliculin* produces it in rabbits, as shown by Karp. Folliculin is unsaturated, lacking iodine (page 211).

Ovarian extracts have been used for the most part as adjuncts to other gland preparations, in human cancer. Ishihara for about 15 years has used a combination of placenta, ovary, and umbilical cord which he calls P.O.U. with animals and in human cancer. The history of his work is gratifying, for, despite the scathing denunciations of cancer experts, including the *American Journal of Cancer*, he has cured so many cases that a hospital has been erected for him in Takamatsu, Japan. Moreover, his work has been corroborated, in part, with animals by Murphy, who has used placental extract successfully. Magian, a British clinician primarily interested in placental extract, has used ovarian extracts as adjuncts for 10 years.

Hoffman, by irradiating the ovaries, was able to induce the disappearance of metastatic nodules from the breasts. (*Surgical Clinics*, N. Am., 1933.)

L. Berman reported in 1931 that he had used a preparation from the interstitial cells of the ovaries, called "ovarian residue," with gratifying success in 12 cases of nodular breasts and 8 cases of nodules in the uterus.

The reason why so little work is in evidence with ovarian extracts, in the treatment of human cancer, is because the complete ovarian substance, with its chemical constituents intact, has had little attention for some years. Faulty methods of extraction and the relative ineffectiveness of those preparations which (we consider) would have small amounts of iodine, have contributed to this. In Berman's cases the iodine action was possible. Thyroid and ovarian extracts combined are sometimes effective.

But the chief point is that synthetic and desaturated substitutes for the true ovarian extract have been under consideration. They are now "fashionable." There are numerous sources of the "sex hormone." *The largest amounts of the estrogenic (female) hormone are secreted in the urine of the stallion.* The placenta is another source. The synthetic compounds include preparations that have Vitamin D potency, cause *cancer* if applied to the skin, and are capable of inducing symptoms of sexual maturity in animals that have been ovariectomized.

For some 25 years, ovarian extracts of greater or lesser value were marketed by some of the pioneers in endocrine medicine. But some of these preparations had little actual potency and probably benefitted by "suggestion."

In 1923, Edgar Allen and E. A. Doisy published the results of their tests with ovarian follicular fluid and lipid extracts from the same. They induced sexual prematurity in young rats at 26 days of age. This work was followed by studies of Loewe (1926) and Zondek (1928) on the female sex hormone from human pregnancy urine.

The *theelin* of Doisy (1929); *progynon* of Butenandt (1929); and *menformon* of Lacqueur have been prepared from human pregnancy urine as crystalline products. More recently, the urine of pregnant mares, and remarkably enough the urine of *stallions*, have been sources of *theelin*, or the *estrone* of several drug firms.

We have elsewhere told of the warnings about sex hormones given by Dr. Edgar Allen, by numerous drug firms themselves, and by the A. M. A. editors and authors. For even *natural* estrogens may be injurious in improper dosage, or administered to the wrong patients.

The newest estrogen, a powerful *synthetic* drug called *stilbestrol*, is remarkably valuable in diseases that are associated with malfunctioning sexual glands. It has been used in ovarian insufficiency, in the syndromes that follow natural or operative menopause, and in the painful breast enlargements of nursing mothers. It is of course important in the production of menstruation in young girls whose adolescence has been delayed. It has also been used in demasculinizing one case of pseudo-hermaphroditism in a 17 year old girl.

In the 126 abstracts on *stilbestrol* (diethyl-*stilbestrol*) issued by the E. R. Squibb Company in 1942, special effort is made to include those which furnish evidence of the *injurious action of stilbestrol in large doses*.

When administered orally, *stilbestrol* has more than 20 times the potency of *estrone*. It may cause nausea and vomiting, however. In some human males, it has been effective in cases of hyper-sexual activity. The fact that it has also produced *gynecomastia* shows that it may be injurious.

In our discussions of the cancer-inducing powers of "theelin," "folliculin," "estrone" and the *synthetic* sex hormones we have been able to cite the cautions that our predominately honest drug firms have always given. If some over-enthusiastic drug salesman, by his propaganda, stimulates a busy doctor to use excessively large doses of a specific gland extract or its synthetic substitute, we should not blame advancing science, or condemn the product.

This brings us to the subject of removal of the ovaries, as a preventative for cancer, in strains of animals that normally have it. It has long been known that removal of the ovaries cures osteomalacia of pregnancy. Blair Bell in his Arris and Gale lectures stressed the fact that the ovaries, by their activity, cause extensive losses of calcium from the body. As we have already indicated (page 170) the early clinicians, of the 1890's and the early 1900's, used ablation of the ovaries, and subsequent *thyroid medication*, as a means of curing breast cancer.

Our first knowledge that removal of the ovaries in young animals would prevent the development of breast cancer in predisposed female mice was furnished in 1916 by Leo Loeb. In his investigations he was able to produce a marked decrease in incidence of breast cancer by removing the ovaries of the young females before the age of 6 months.

Later Cori, in 1927, found that in cancerous strains of mice operative removal of their ovaries when they were from 15 to 20 days of age prevented females of that line from developing mammary cancer. Even up to 6 months such procedure reduced cancer incidence.

In 1938, Murray, extending the studies, produced mammary cancer in male castrated mice by transplants of the ovaries of their sisters. He also found that in a line of mice where 80% of the breeding females developed cancer of the breasts, it was possible to keep virgin females from mating, and to reduce the cancer to about 11%. Cancers were delayed in their appearance in such animals as developed them.

The ovaries consist of fatlike and fatty substances, and normally seize iodine from the blood and retain it in considerable amounts. The adrenal cortex, richest in cholesterol of all the glands of internal secretion, is also an iodine-binding structure. In fact, the ovaries,

the adrenals and the anterior lobe of the pituitary all contain cells of similar lipoid type, and iodine in appreciable amounts.

That the cholesterol of the adrenal cortex is an essential to its function is indicated by the fact that after the adrenals have been operatively removed, masses of cholesterol implanted in the body of the animal will prevent Addison's disease. Addison's disease, which was until recently fatal, is caused by impaired function of the adrenal glands in their cortical portions. It has been experimentally induced by operative removal of the cortex of the adrenals, and has been treated successfully in animals and in human cases by extracts from these glands. Notable is the fact that the use of thyroid extract or iodides in excess will hasten death in experimental animals that have lost their adrenals. Their "Addison's disease" is rapidly fatal. Our conclusion is that since cholesterol implants and other experimentally introduced substances of benefit are "unsaturated," the normal function of the *cholesterol in adrenals is to serve as a reservoir for iodine*, which is released in times of stress and strain to aid in the removal of lactic acid from the muscles, and also to facilitate rapid coagulation of the blood. This set of manifestations discussed by Cannon in his book, "Bodily Changes in Pain, Hunger, Fear and Rage," is not, however, limited to the adrenal glands alone, but involves also the release of iodine from several other glands of internal secretion, including the anterior pituitary, the thyroid, and the parathyroid glands.

While early students of the effects of ovariectomy had noted apparent protective action against breast cancer, but had not identified this action with the similar benefit reported in the cases of unusually heavy losses of calcium in pregnancy, we believe that the evidence is conclusive to show how in both cases the conservation of essential elements is achieved by glandular behavior. For overactive thyroid glands precede the osteomalacia (heavy calcium losses) of pregnancy, and, as we have elsewhere explained, also precede the development of breast cancer in human males.

When Dr. G. Wooley, of the R. B. Jackson Memorial Laboratory, Bar Harbor, Maine, demonstrated in 1940 and 1941 that the adrenal glands of ovariectomized female mice and castrated male mice became hypertrophied, and that in some cases these animals developed cancers of the breast, despite the fact that they had lost their ovaries or testes,

he added a most important fact to our knowledge of operative effects.

He removed the ovaries of 82 mice soon after birth, and naturally expected that none of this lot (from a strain that inherited breast cancer) would have mammary cancers. But 22% of them did develop it. The breasts and the secondary sex organs were at first atrophied, and then they began to grow, shortly before the breast cancers developed. The adrenal glands of these animals had apparently altered in their function, and the "substitute hormones" took over the determination of the secondary sexual characters of the females. The uterus, vagina, and the mammary glands of the females seemed to develop satisfactorily, despite the loss of the ovaries, in animals that did show enlarged adrenal glands. In the males, Wooley reports (February, 1941) that there appears in some cases marked enlargement of the breasts, and even, in a male that had been castrated at birth, two breast tumors developed. The adrenal glands enlarged before the mammary glands in operated males began to resemble the breasts of female mice.

Wooley, Fekete and Little have further reported (*Science*, March 26, 1943) that when mice were ovariectomized or castrated at 2 days of age, a very high percentage of them developed *carcinoma of the adrenal glands*.

Wooley and associates cite the fact that injections of the estrogenic (female sex hormone) hormones have caused tumors of the testes, uterine cervix, pituitary gland and mammary glands in mice. They consider that hormonal imbalance is one of the factors leading to this type of cancer.

Our interest in this phenomenon is in the fact that the operative removal of any of the sets of glands of internal secretion is known to cause chemical changes in others, showing that iodine is absorbed by the remaining endocrines. If the anterior pituitary gland is removed, the iodine of the thyroid gland increases; in castrated horses (geldings) the thyroid contains 55% more iodine than in stallions (Klein, 1921); in castrated (ovariotomized) female rats, Bocklemann found the thyroid gland contained much more iodine than in normal females.

The typical hyperplasia (enlargement) of the adrenal cortex which Wooley secured after ovariectomy or castration in mice has been induced by the feeding of pituitary substance, and also by thyroid feed-

ing. Not only do chemical analyses show that the adrenal cortex is rich in iodine (Chidester, *Archiv. int. de Pharmacodynamie et de Therapie*, 1934), but tests with tadpoles indicate that the adrenal extracts will hasten metamorphosis, just as thyroid extract does. Finally, we have the studies of Black, in 1922, who used adrenal extract to cause a 70.4% gain in the iodine content of the thyroid gland in dogs.

The anterior lobe of the pituitary gland yields an extract that is well known to be *thyroid-stimulating*; and this extract is the cause of enlargement of the adrenal cortex, when injected. From all these facts it seems that the adrenal cortex is not only rich in cholesterol, but that it absorbs iodine from the body fluids.

The disease known as Addison's disease, identified by clinicians as due to pathological conditions in the adrenal cortex, has been experimentally induced in animals by operative removal of the adrenal cortex. The extracts from adrenal glands used for the past 14 years with experimental animals, and for about 10 years in human cases, have saved many lives. In an important study Harrop has been able to improve the condition of experimental animals suffering from Addison's disease by implants of cholesterol in the form of pellets. Dr. Arthur Steinberg informed this writer that he has used successfully "unsaturated substances," which share with cholesterol that quality. We have discussed the role of unsaturated substances elsewhere in this book (page 207). It is significant that an unsaturated substance may be extremely valuable in seizing iodine, as for example in the case of adrenal cortex loss; that it may also be valuable in restoring fertility, as exemplified in the case of wheat germ oil; but that it is injurious when it accumulates in excessive amounts in blood vessels, gallstones, cataracts, or in tumors.

Joannivics has shown that the removal of both adrenal glands in mice causes the regression of tumors. We can see how such operative action would permit the iodine that might otherwise be greatly in excess in the body to unite with the unsaturated fats and lipoids of the tumors, and cause their rapid breakdown. The tumors could actually, by their cholesterol and other unsaturated substances, protect the mice for a time against Addison's disease.

We know that cholesterol in the adrenal cortex will seize and retain iodine, just as that in the ovaries does. And we know that long-continued overactivity of ovaries or any other glands of internal secretion will cause heavy losses of the protective elements, the cancer-preventing elements, including iodine and calcium. Thus, the adrenal cortex could and did, presumably, take over a function that had been lost. Implants of several different glands are known to cause experimental cancer. We believe that they do so by incessant disturbance, which exhausts the glandular protective mechanism.

Murray has paired male with female mice that were of a breast cancer strain by uniting (anastomosing) their blood vessels and placing them so the union was undisturbed. Neither animal in a pair developed breast cancer. This may have been in part due to chemical differences and in part to the operation, which activated glands.

There are hazards of uterine cancer in women of races which marry young and have a number of children. But there is also danger of breast cancer developing in mothers who do not nurse their babies. Occlusion of the ducts paves the way for cancers.

In unmarried women, cancer of the breast may occur, due to disordered sex cycles. Ingleby of Philadelphia has given us cleancut evidence that in women, as well as in experimental animals, disturbed sex cycles cause cysts to appear in the breasts. The intimate relationship between the pituitary, the thyroid, the sex glands and the breast has been emphasized already. It is worthy of mention that with mental stress and strain some women have noted the rapid growth of their breast tumors. *Excretion* instead of *use* of the essential elements comes with glandular overactivity, and this overactivity has been induced by disturbed mental states, we know.

The synthetic sex hormones are known to induce cancers, and there is danger unless any of these unsaturated hydrocarbons is guarded by iodine. Certain clinicians always give iodine with them (page 167). P. H. Wood (*So. Med. J.*, 1932) regularly gives thyroid extract with *theelin*.

Lacassagne of Paris, in 1933, informed us of his successful production of experimental cancer by means of injections of folliculin, the female sex hormone. He gave fortnightly treatments to young *male* mice, and induced in them typical breast cancers.

After 23 days of estrogen administration, Geschickter was able to produce mammary cancers in rats. In several instances these disseminated as metastases to the mediastinal lymph nodes and to the lungs. (*Science*, 1939, vol. 89, p. 35.)

Similarly, Noble and associates used oestrone tablets to produce mammary cancers in rats. (*Can. Med. Assoc. J.*, 1940, vol. 42, p. 413-.)

The action of various estrogenic hormones in causing the mammary glands of male animals to become functional and then to develop cancers reminds us of the action of a goitrous thyroid, which in men precedes human gynecomastia. And we must also point out the fact that the same hormone which induces breast cancer causes a change in plumage in castrated male fowls to that of the females. Such plumage changes, and such stimulation of breast function, are also known to be due to thyroid extract feeding as well.

In discussing the reports of human breast cancer in males with a history of gynecomastia, Dr. C. F. Geschickter has assured the writer that in all the records available to him regarding enlarged breasts in very young boys and girls there was no indication that they later developed breast cancers. Close supervision of such cases and early treatment have been made possible by parental interest in the excellent school health inspections that we have in the United States.

It is unfortunate that some investigators of cancer problems that involve the glands of internal secretion know so much that is not so about these glands. For the real key to their behavior is, as we have long ago shown, due to the iodine in them. And the use of desaturated substances merely activates the iodine-rich glands, exhausting them rapidly.

Other Glands or Structures

Placenta

In 1931, Gross described his experiments in which human placental tissue retarded the growth of tumors. It is well known that the elements necessary for nutrition of the embryo, passing through the placenta, are retained by it in considerable amounts and liberated gradually. Doederlein has identified the thyroid secretion of the mother with placental tissue; de Re and de Nunno, in independent

experiments, have used placental tissue to hasten tadpole metamorphosis, a common test for iodine.

We have mentioned the combination of placental extract, ovarian extract, and the umbilical cord, used by Ishihara for the past 15 years in animal tests and with human cases of cancer. His P.O.U. hormone is given by mouth, and by injection. In more than 200 cases of carcinoma he has been able to secure marked improvement, and many have been permanently cured. This writer began his correspondence with Dr. Ishihara in 1934, and has been much gratified to learn that he has taken over, as an adjunct, the administration of *calcium*, which we advocated in our early papers. These papers are in the loan library of the American Medical Association, and are in use by some clinicians. Probably the failure of some cancer men to secure favorable results with P.O.U. may be attributed to faulty supportive treatment.

A. C. Magian, of the Royal Institute of Public Health, London, has been using a combination of placental extract with sera and blood transfusions, in human cancer, for about 10 years. He also gives the male patients testicular extract; and the women, ovarian extract, in addition.

Magian injects fresh extracts from human placenta deep into the muscles. He supplements with the sex gland preparations according to the sex of the patient, and also uses blood transfusions. Even inoperable and hopelessly incurable patients have been benefited in late stages. Magian considers his treatment to be valuable as an adjunct to surgery and radiant energy treatments, and that it improves the patient's chances for life, and even cure, by about 25%. Surely the treatment has sound chemical basis for being valuable after the major attacks by radiation or surgery. For the placenta strains out and transmits elements that we know are needed in all wasting diseases, influencing metabolism.

Murphy and Sturm, in 1933, found that placental extracts from mice inhibited growth of experimental cancers. They also used embryonic skin with similar benefit. It is generally known that *skin extracts* increase resistance to disease, and Milbradt identified this with the same reaction to methyl cyanide, produced by thyroid extract, and called the "Reid Hunt reaction." Chemical analyses of

skin and placenta indicate that their iodine content may be involved in cancer inhibition.

Spleen

In 1910, Bayer reported that fresh beef spleen caused some inoperable tumors to degenerate, when gland and tumor were sutured.

Woglom (*J. Exp. Med.*, 12, 29, 1910) was able to inhibit the growth of inoculated tumors by implanting spleens from animals that had been previously inoculated with tumor tissue.

In their 1922 experiments on transplantation of organs, Murphy and Sturm learned that grafts of the spleen from rats, transplanted into the brain in the region adjacent to implanted sarcomas, prevented the transplants from growing. Whether this was due to the demand of the spleen substance for elements and growth substances needed by the tumors, or due to the carcinolytic elements from the spleen, we do not know. But we do know that the spleen is rich in iodine.

Burghardt, in 1929, reported spleen preparations beneficial in human cancer.

Reeke, in 1930, found that spleen substance inhibited growth of cancers. But clinical reports do not convince research men, limited to surgery and radiation.

In 1932, Buengler, who tested a variety of gland extracts, learned that splenic extract prevented growth of tumors, and also inhibited lactic acid formation. Extracts from lymph glands, testes, thymus, lungs, and heart were slightly inhibitory in the animals tested.

Fischera, in 1933, reported on 20 years of clinical experience in cancer with extracts of organs. From 1930 to 1933 he treated 300 cases of cancer by injections of spleen, thymus, lymph glands and bone marrow. He cites chemically induced cures of 9% of his inoperable group of 100 cases. But his records for long-time complete cures are not available. His method was not suggested to supplant surgery or radiant energy. He made experiments with rats before trying his extracts on human cases. In the spleen, the growth of rat tumors was inhibited; in the testes and ovaries, these implants grew rapidly. Fischera's technique included the preparation of extracts of the organs from freshly killed calves, which were kept in an incubator from 1 week to 2 months. The dosages ranged from

1 to 2 cubic centimeters intramuscularly, and in some cases intravenously.

Recent experiments (1939) by Lewisohn and associates of the Mt. Sinai Hospital, New York, were reported as successful in 80% of transplanted tumors, which regressed when a concentrated spleen extract was used.

The spleen is engorged with blood in animals at each mealtime, and it is richer in iron than livers. There is an argument in favor of spleen as a food especially in anemic, cancerous and tuberculous patients, we believe. And after radiation the iodine, iron and calcium of the spleen will be extremely valuable. (See pages 138, 144.)

Bittner reports that transplantation of splenic tissue from mice of strains with high incidence of *mammary cancer* will promote the development of this type of cancer in recipients of the transplants. (Bittner, U. S. Public Health Report, 1939, 54, 1927.)

This may be an instance of a generally lowered resistance to cholesterol accumulations caused by the glandular upset induced by transplants, for hyperthyroidism precedes cancer in many cases. (See page 172.) It also occurs prior to *gynecomastia* and cancer of the male breast. (See page 118.)

Bone Marrow

Rosenstern and Köhler (*Lancet*, 1932, ii, p. 42, Berlin correspondence) used alcoholic extracts of bone marrow, and injected into a group of patients with rectal, esophageal, and gastric ulcers, and cancers. In four cases, absorption of the growths took place and weight increased.

Mammary Gland

Extracts from the breasts of women with mastitis (inflammation) have been used with some degree of success to reduce the toxic manifestations.

L. Berman, in his 1931 report, summarized the benefits derived in 18 cases of bleeding nodular uterus treated with mammary gland extracts. He did this because he had noted that during active lactation periods uterine fibroids grew smaller. As we have elsewhere indicated, lactation is marked by an increase in the blood iodine

of as much as 120% more than at other times. The colostrum contains large amounts of iodine in cows and the human female.

Iodine in the Glands of Internal Secretion

"Things true and evident must of necessity be recognized by those who would contradict them."

—EPICETUS

In 1917, Professor E. Gley, of Paris, in his book on Internal Secretions, emphasized the fact that with some preparations the doses of glandular extracts necessary to produce characteristic physiological effects were so large that they represented in weight the masses of several of the glands. He asked, "Is it not plausible that this action depends on the presence of a substance which occurs in all these extracts, consequently a substance that is widely distributed, and therefore general, rather than specific?"

The author has been a student of iodine and of glands since 1912, and has published numerous articles illustrating the rôle of iodine in glandular therapy. In 1934, he set forth the fact that iodine is the "substance" sought by Gley, in a paper published in *Archives Internationales de Pharmacodynamie et de Thérapie*, vol. 48, Fasc. III et IV, entitled, "The relation of iodine to the effectiveness of endocrine extracts."

Gley had shown in 1897 that the parathyroid glands were reservoirs of iodine, with 35 times as much iodine as in the thyroid in proportion.

Analyses by Maurer in 1928 showed that the iodine content of the thyroid gland of the rabbit was 15,800 parts per billion; and that the ovaries, uterus, spleen, bile, liver, had diminishing quantities. Recently the Lahey Clinic group have also shown that the ovaries are next to the thyroid in their iodine content, containing twice the amount found in any other gland except the thyroid.

Ruff, in 1933, analyzed glands in cattle, and cited the order of iodine content as thyroid, spleen, adrenals, testes, ovaries, pancreas, liver and pituitary.

In the study made by Kato, in 1936, with normal untreated rabbits, he placed the thyroid first, then the pituitary, the adrenals,

and the ovaries. Kato also tested the ability of various glands to absorb iodine, after heavy dosage of the rabbits.

Iodine is present in such amounts in other glands, and also in placenta, umbilical cord, bones, muscles, and in all natural sources of sex hormones, that we must consider it as important in any extract that may be made from these structures and used in tests on growth, reproductive maturity, or cancer.

Iodine in the Human Body

Sturm and Buchholz, in 1928, made special studies of the quantitative distribution of iodine in the human body. They showed that the total iodine amounted to about 51 milligrams. This, according to the terminology in general use, would be 51,000 gamma. Gamma represents a millionth of a gram, or 1/1000th of a milligram.

Of the 51,000 gamma of iodine, $\frac{1}{2}$ (25,150 gamma) appeared in the muscles; $\frac{1}{5}$ (10,234 gamma) in the thyroid gland; $\frac{1}{10}$ (5250 gamma) in the skin; and $\frac{1}{17}$ (3000 gamma) in the bones.

In his book, "Iodine Metabolism and Thyroid Function," A. W. Elmer, of Lwow, Poland, has given tables indicating the results of iodine analyses by various investigators for the tissues of man, the dog, the rabbit, the guinea-pig, and cattle. He has referred to our own papers on the relationship between the functioning of glands of internal secretion and the iodine content of these glands.

Let us compare some of the high iodine determinations for human glands. Sturm lists the thyroid as 29,400 gamma; spleen—429; adrenals—393; parathyroids—385; testes—165; ovaries—160; liver—118. Other analysts have listed the ovaries next to the thyroid in their iodine content (Maurer, Perkin). It is well known that follicular liquid contains iodine in large amounts. The cancer-producing "folliculin" is, however, a *desaturated* hydrocarbon, without iodine. (See page 189.)

There is great variation in the reports of analysts for the liver, kidneys, lungs, and skin, since these organs excrete large amounts of iodine, and they have been studied during periods of greater or lesser iodine excretion.

Elmer, from his own analyses, reports the high concentration of iodine in the *adrenal cortex*, which he relates to the functional connec-

tion between the thyroid and the adrenal glands. Of the pituitary he says, "The *anterior lobe* of the *pituitary* has a high concentration of iodine, which may very probably be associated with the functional interrelationship between the anterior pituitary lobe and the thyroid."

Cancer implants are unsuccessful in the *spleen*, a gland that is regularly engorged with blood at each mealtime. Great variations in the reports on iodine in the spleen exist, and Justus, in 1904, and Sturm, in 1928, record definitely high concentration of iodine in it.

Similarity in effect of certain insulin-like plant products that are rich in iodine (water-cress) and of iodide of iron, in diabetic cases, to the influence of insulin has been pointed out by the present writer in a number of publications. The pancreas has appreciable amounts of iodine in it, and we have recently been informed that the *whole pancreas* yields an extract that is superior to insulin in some respects in diabetes.

The simultaneous combustion of fats and carbohydrates, which is facilitated by the pancreas and the liver, seems necessary for health, and such combustion is believed by Shirlaw to prevent cancer. Iodine here plays an important rôle.

Elmer has shown that, in contrast with the general depletion of iodine in the body, pathologically altered tissues show a greater iodine content than the normal ones. Tuberculous tissue of the lungs shows a higher iodine concentration (142 gamma %) than the surrounding normal pulmonary tissue (62 gamma %); cancerous tissue shows a concentration of 79 gamma % while the normal tissue surrounding contains 24 gamma % (Buchholz and Sturm, 1928).

After iodine administration, a greater accumulation of iodine is found in pathologically altered tissues, tuberculous, syphilitic, sarcomatous, cancerous tissues than in surrounding normal tissues (O. Loeb and Michaud, 1907; Takemura, 1911; Van den Velden, 1908; Lewis and Kraus, 1914; Holler, 1923).

The iodine level in the circulating blood is markedly increased during menstruation. In some cases it rises in the first day to 40 gamma %. Maurer and Diez, and Leipert, independently recorded blood iodine increase to be high, about 110%, at menstruation. E. Gley first observed that menstrual blood itself was markedly increased in iodine content. Jahn and Kesselkraul (1928) believed that the

shorter the menstrual period the higher was the iodine concentration in menstrual blood.

In our discussion of Ingleby's remarkable studies (page 123), we have shown how iodine and potassium will bring to the mammary glands of women in the intermenstrual period larger and larger amounts of fats, lipoids and growth-acids, and that thus the growth of tumors in the breast increases up to the time of menstruation. From clinical and experimental evidence it is clear that the 110% increase in iodine and a similar rise in potassium in the blood which occur at menstruation will cause rapid dispersal of the lipoids, fats and growth-acids of tumors. Here nature has a check against metastatic dispersals, for the thyroid gland is overactive at menstruation, and calcium is found in the blood in increased amounts at that time. Such calcium tends to prevent metastases. The writer is of the opinion that irradiation of breast cancers (before operation) is a cause of metastatic spread, because activated iodine and potassium will break down the new growths too rapidly.

CHAPTER XII

Chemistry of a Cancer

The blood contains salts, balanced just as in sea water, and it brings to all the cells and tissues the derivatives of foodstuffs. These include proteins, carbohydrates, and fats, in assimilable form. Blood transports oxygen through its combination with iron in the red corpuscles. Its white corpuscles convey foodstuffs, and some of them are able to engulf bacteria and carry away foreign matter that might otherwise accumulate in the region of injuries.

Lymph bathes every cell in the body, and mediates the interchange between tissues and circulating blood. The lymphatic system has certain glands in it which are especially prone to be attacked by metastatic masses from cancers. Like the liver, the lymph glands serve as strainers for potentially injurious matter. Lymph is similar in composition to blood, but it coagulates more slowly, it lacks red corpuscles, and its circulation is sluggish, as in higher animals there are no "lymph hearts," and intracellular pressure aids in its transportation. Lymph glands become infected early.

In cancers there are gathered the amino-acids, fatty acids, lactic acid, and various lipoids which are found in normal tissues. Also we find with them the essential elements from blood and lymph that are carried all over the body. The differences between cancers and other structures are not so great as we might conjecture. Their cells merely run wild in growth. They are, however, very like normal cells, rapidly growing.

Several of the amino-acids, experimentally proved to hasten the growth of experimental cancers, are known to be inactivated by iodine. This is true of glutathione and its individual amino-acids. It is known, too, that after the thyroid gland has been removed glutathione in the blood increases, while with thyroid overactivity glutathione is decreased.

Oxygen lack is favorable to the conversion of starches and sugars to lactic acid in cancerous tissues. And the lactic acid, notably present in young, rapidly growing tumors, aids in the destructive action of these growths upon surrounding tissues, for lactic acid penetrates cells quickly. A lack of calcium favors lactic acid effects, and calcium is low in the blood of cancer patients. (See page 116.) Experimentally, iodine prevents lactic acid formation.

Unsaturated (iodine-free) fatty acids are circulated in the blood and are present in rapidly growing tumors in greater proportions to cholesterol than in the slowly growing ones. Lecithin, which is present in egg yolk and liver in quantity, consists of a number of unsaturated fatty acids, and is favorable to the higher water content of some malignant growths. Tests with unsaturated fatty acids show that they accelerate the growth of tissue cultures as much as 150% and that they actively stimulate experimental cancers. But when iodized the fatty acids no longer exert these effects.

Penn (1935) has reported favorable results obtained in inoperable malignancies by the use of phospholipins. Lecithin is a phospholipin.

He finds that cholesterol in an abnormal amount may interfere with cell function due to the disturbance of the cholesterol-lecithin ratio.

Cholesterol, a lipoid (fatlike) substance, related to the higher alcohols, is found in large amounts in the most malignant cancers. It normally accumulates in the brain, the ovaries, the adrenals, and in other glands of internal secretion. A heavy fat diet of eggs and milk, bringing cholesterol, will cause arteriosclerosis in young children.

This fact was discovered when such diets were given to young diabetics. Cholesterol constitutes a large proportion of the constituents of cataracts, gallstones, arteriosclerosis and cancers.

Removal of the thyroid gland increases cholesterol deposits in the body. The simultaneous administration of cholesterol, with iodine, does not result in experimental arteriosclerosis if the thyroid glands of the animals are functional. But cholesterol without iodine will cause such arteriosclerosis. Iodine is activated by *sunlight*, and the prolonged effect of the sunlight is to alter the chemistry of the skin and permit unguarded cells to grow excessively and form a

cancer. Heavy sunning will also cause severe thyroid disturbances, and thus lower resistance, permitting cholesterol accumulations.

The Schultz reaction differentiating malignant from benign tumors is based entirely on the excess of cholesterol within the neoplasm.

In the skin, sun exposure and ultra-violet light irradiation will act on the cholesterol and hasten development of skin cancers, as shown by Roffo, of Buenos Aires. According to Roffo "the cholesterol content is more concentrated in those skin regions which show the greatest tendency towards tumor development." (*Am. J. Cancer*, vol. 17, January 1933.)

A. P. Mathews says, "The inhibitory effect of cholesterol on lipolytic enzymes is a well-known physiological fact" (Mathews, *Physiol. Chem.*). This may account for the "disturbance of fat metabolism in the presence of malignant diseases, and the inability of cancer patients to split fatty acids of high molecular weight" found by Pourbaise and Byutart.

Proliferating cancers have high sodium and potassium and low calcium and magnesium contents. *Calcium* is high in slowly growing or regressing cancers. Growing tumors have some iodine; *regressing tumors have large amounts of it*, by analysis. We have elsewhere discussed the importance of iodine in preventing cancer and in curing it. For an evaluation of the rôle of the elements, see pages —.

If glands of internal secretion are functioning normally, and if the diet is adequate, there will be growth control, and cancers will not normally arise.

There are certain hydrocarbons that are able to overcome the protective elements in spite of limiting factors. These we will now discuss as "Unsaturated substances which induce cancer."

"But when ill indeed,
E'en dismissing the doctor don't always succeed.

—G. COLEMAN

CHAPTER XIII

Unsaturated Substances which Induce
Cancer

Since 1930, about 45 definite chemical compounds have been discovered which are capable of inducing the growth of tumors in experimental animals.

In 1929, when Yamagiwa and Ichikawa reported that coal tar applications induced skin cancer in rabbits, they made a tremendous advance in the field of experimental cancer. Ether extracts of coal tar also cause cancer; and ether-extracted chimney soot has also proved carcinogenic.

Hydrocarbons from shale oils and oils from petroleum wells were tested by certain investigators at Manchester, in 1930, after evidence had accumulated to show that men who were splashed with lubricating oils from spinning machines had developed cancers. The most highly refined oils were the most active in causing spin cancer in mice. These oils are now treated to render them harmless. The ordinary method is by hydrogenation. This saturates the *unsaturated* hydrocarbons.

The Tworts reported that "The carcinogenic constituents of mineral oils are probably unsaturated benzenoid hydrocarbons." Studies by Lyth in 1933 attempted to link the refractive index with carcinogenic activity. He said, "When the refractive index of the oils was below 500, they were of low carcinogenicity, but when it was above 600, they became carcinogenic. The shale oils with the *highest iodine numbers* were the most toxic."

The "highest iodine numbers" simply means that these oils would take up the largest amounts of iodine when it was added to them. And the agents which render these oils ineffective in causing cancer are those which make it impossible for them to take up iodine.

Later work by Kennaway's staff in London has extended these findings and a number of *hydrocarbons* of an unsaturated nature

proved to induce cancer, when applied to the skins of mice. They are linked chemically with the sterols. When a sterol is de-hydrogenated, it becomes cancer inducing. When a substance has *lost* hydrogen it can accept *iodine*.

Several of the sterols that have been used to treat rickets are also cancer inducing. Some of the earliest workers with sterols in Vitamin D deficiency recognized that they were unsaturated, without realizing the physiological significance. When these sterols were *brominated*, and thus saturated, they were incapable of demanding iodine and thus causing an activity of the glands that control calcium deposition.

Since 1933 the writer has reversed the usual policy of secrecy in his correlated and experimental work, and has done his best to place before men who were able to run laboratory tests any correlated facts which they might use. The result has been largely in the *clinical* use of his material, and reports have come from this and foreign countries which indicate the successful addition of minerals (calcium, iodine and iron) and normalization of the protective endocrines in several diseases. Before the present war, letters were received from Ishihara (Takamatsu), Stepp (Breslau), and others in Norway and in France, showing that our emphasis on restoring mineral-vitamin-gland balance had been useful in prenatal care and in cancer.

We have identified the gland-balancing power of a cod liver oil, rich in *iodine*, as significant in rickets and also in *anemias*, because, as W. G. MacCallum (pathologist at Johns Hopkins University) first showed, calcium and iron are laid down in the bones together. If we conserve calcium, we conserve iron. Insulin, deemed valuable in some anemias, and cited as useful in cancer, *slows down* the over-active thyroid, conserving the calcium, iodine and iron.

It is highly significant that the pioneer work of McCarrison on the fat-thyroid-iodine balance, which clearly showed the need for *iodine* with oils and fats furnishing Vitamins A and D, has been completely ignored by everyone but this writer and one textbook author (M. Withrow Morse, "Biochemistry"). As we have indicated (*Int. Clin.*, 1934) the early studies of McCarrison and of Mellanby on *goiter* and on *experimental rickets* showed how necessary iodine was in the cod liver oil that normalized the thyroid in goiter.

The action of *unsaturated substances*, when fed, may be injurious,

or beneficial, depending on various factors. In the classic studies of McCarrison, 1919, he showed that oatmeal and wheat germ would cause goiter in experimental animals, but that cod liver oil, because of its considerable iodine content, was able to restore the gland to normal, and to induce a "fat-thyroid-iodine balance." Later, 1921, when Mellanby used cod liver oil to restore to normality dogs that had developed rickets, he failed to evaluate the principle of McCarrison, or to consider the fact that hyperthyroidism causes enormous losses of calcium. In fact, he went so far afield as to attribute to wheat germ and oatmeal certain *toxic factors* in their unsaturated fatty acids. He forgot about the thyroid.

We have interpreted the "toxic factor" of Mellanby as the action of unsaturated fatty acids on the thyroid and other glands that control calcium (*Int. Clin.*, 1934). After hyperthyroidism, which causes the loss of 250% more calcium, rickets would result. The value of *irradiated sterols* in rickets is in part due to their unsaturated nature and in part due to the effect of irradiation of stores of iodine in the body. But, as demonstrated repeatedly, cod liver oils with considerable (naturally contained) *iodine* prove superior to sterols in rickets.

Mellanby has not indicated in his later papers any knowledge of reprints sent him on our rickets study (*Int. Clin.*, 1934) and cancer, but he may have been impressed by our articles on cancer, or those of his countryman, Dr. Stevens. In any case he has successfully used *iodine* and potassium permanganate in inactivating the Rous chick sarcoma (*Nature*, 1938).

Similarly Marine and associates (1929) found that fresh cabbage did not cause goiter in rabbits, while cooked cabbage was goitrogenic. Here, iodine had been driven off, and the unsaturated residue would of course demand iodine, and stimulate the thyroids of the animals fed.

Natural cod liver oil, rich in iodine, is the safest normalizer of the glands that control calcium. Excessive Vitamin D from either the sun (see page 92) or from irradiated substances of an unsaturated nature proves very dangerous. Some Vitamin D preparations are cancer forming.

A similar situation has arisen with reference to the effect of *unsaturated* cancer-inducing hydrocarbons applied to the *skin*. The

"mystery" is still unsolved it seems. Yet, in the absorption of protective iodine by unsaturated fats or hydrocarbons there seems no mystery. And if the iodine which is needed to prevent new growths is already absorbed, such growths will occur. We must not overlook the profound derangement of the glands of internal secretion which may occur through excessive amounts of unsaturated substances, and which may cause general glandular overactivity, hasten systemic exhaustion and internal cancers besides inducing *local* effects wherever applied.

Dr. W. Mitchell Stevens, of Cardiff, with whom the writer has been exchanging reprints and letters since 1935, has recently stressed the fact that the carcinogenic agents developed by Twort (1931) and Lyth (1933) in their research on shale-oil hydrocarbons and skin cancers in mice were those with the *highest iodine numbers*, and that chemical saturation of the agents eliminated the carcinogenic effect. (Stevens, W. M., *British Medical World*, Oct. 17–Nov. 28, 1941.) It is reasonable to suppose that Dr. Stevens independently arrived at this conclusion. For Dr. Stevens concurs with the writer on many points in which iodine is related to normal growth and the prevention of cancer.

Although both Twort and Lyth mentioned the unsaturated nature of their cancer-inducing hydrocarbons and the fact that the shale oils with the *highest iodine numbers* (and greatest demand for iodine) were the most toxic, this writer is the only person (until Dr. Stevens) who correlated this fact with the profound action of unsaturated substances on the iodine reservoirs of the body. The local effects of repeated application of the unsaturated or desaturated shale oils include the rapid absorption of iodine which would normally protect against "new growths."

The reviewers of Twort and Lyth and the later workers with hydrocarbons that induced cancer have all, like these workers themselves, emphasized the fact that the *refractive index* was very high in the most toxic substances. American and British reviewers have stressed the refractive index and failed to mention the unsaturatedness, as in Science News reports (Science Service).*

* Citing "Advances in the Sciences during 1934," Science Service (*Science*, December 28, 1934) stated, "The cancer-producing property of mineral oil is

Our first discussions of the significance of unsaturated substances appeared in separate papers on iodine and the endocrine glands, cancer, rickets, and the sex hormones, published in 1934. In 1935, we published a general resumé, "Dehydrogenated and unsaturated substances in relation to cancer, vitamins and hormones." (*Med. World*, 1935, vol. 53, No. 3, pp. 167-172, March, 1935.)

The author has been a student of the endocrine glands since 1912, and was unusually fortunate in being able to ask expert biochemists to explain the intricacies of behavior of unsaturated substances in the test-tube. The research work of cancer students has been seriously retarded in its progress by their failure to realize that it was *not* the refractive index of the carcinogenic hydrocarbons but their *unsaturated nature* which caused cancer.

In 1933, a feeling of breathless suspense lest others also should have seen the direct relationship of the unsaturated nature of the cancer-inducing hydrocarbons preceded our publication of a number of medical journal articles. In these we indicated how such substances would absorb and overpower the protective iodine in a given area of the skin, and hasten tar cancer and shale-oil cancer, besides causing general glandular unbalance as well. After a time, when no one else subscribed to the thesis, we experienced sadness at their lack of perception of the simple growth-processes involved. Despite efforts to induce others who were strategically situated to perform clinching tests, we have been unable to stimulate them. It seems likely that numerous friendly investigators have waited in the hope that the writer might be able to demonstrate his thesis first.

Unsaturated substances are able to stimulate iodine reservoirs, and to benefit cancer, already present; they may act as *sex hormones*, through mobilization of iodine; they may offset an unusually large amount of iodine in animals that have been starved of fats and thus (as "Vitamin E") benefit sterility.

Prior to the important studies of the late Edgar Allen on the ovarian hormone, certain ovarian extracts had been made that varied

related closely to the oils-refractivity constant, Dr. C. C. Twort and J. W. Twort, Manchester, England, found; they suggested that selection or treatment of lubricating oils with this fact in mind may result in lessening of skin cancer among textile workers, known as mule spinners cancer."

widely in their real worth. Undoubtedly some of those secured from the ovaries of the *hog* were, as Lorand has reported, especially valuable because they had *more iodine* in them than extracts from the ovaries of cows.

As Allen has told us (*J. A. M. A.*, 1940, vol. 114, 21, 2107-2114) in his first extracts the follicular liquid was aspirated from the follicles of ovaries, taken at a meat-packing plant. Allen states, "One of the remarkable things about that first experiment was that all the animals injected gave positive results" (the stimulation of immature females to sexual development and function). Such an extract would be iodine-rich and *naturally balanced*.

The later preparations of a *synthetic* unsaturated nature were soon in general use experimentally and clinically but they proved *dangerous*, since they produced cancer in animals and in human cases.

Realizing that clinical findings and experimental tests had shown that the natural sources of the "sex hormones" were the safest, and that iodine was the key element, found in the ovaries and the testes, and liberated from the midbrain and the pituitary gland, under sexual excitement, we prepared a paper that set forth these facts, and also emphasized the dangers of cancer from synthetic "sex hormones." (See Chidester, 1934, "Anterior pituitary hormone and other preparations influencing gonadal activity." *Med. Record*, vol. 139, pp. 591-596, 641-642, June 6 and 20, 1934.)

It is a commentary on our American way that the editor of the *Medical Record*, who was consultant to a drug firm, had issued, previous to his acceptance of the MS., a long report of his own clinical experience with the very sex hormones that were adversely criticized in my paper. Yet he was willing to publish the *other side*. Later developments have justified this fair and broad-minded attitude.

It is pleasant to record the fact that Dr. Allen read this and other reprints of the writer which were most critical of sex hormones that lacked iodine, and wrote that he was using them in his seminars at the University of Missouri.

Later he exhibited keen interest in the desire of the writer to test the effects of iodizing theelin in experimental cancer, and tried to further such a research project.

In his address (1940) he said, "After the demonstration that

estrogenic treatment, long continued at high levels, is followed by abnormal growths of the female genital organs, including fibroid tumors of the uterus, cervical carcinoma and mammary cancer, the following question may be asked: 'Is the clinician justified in prescribing enormous doses of concentrated estrogenic preparations for aging women?'"

In their diligent and unselfish efforts to prepare new and highly potent and inexpensive synthetic sex hormones, numerous scientists have produced substances as potent as dynamite and almost as dangerous. For they have, by extracting and discarding the *iodine of natural glandular extracts*, destroyed the protective, normalizing element which is responsible for the proper functioning of the sex glands, and which guards against injury through unsaturated lipoids and acids.

The synthetic preparations, not only lacking iodine but highly desaturated, were very stimulating on the iodine reservoirs of the body, and did, thus, cause sex gland activity, but they were so very powerful that speedy exhaustion of the endocrines resulted, and cancers developed.

It is unfortunate that many physicians are still unacquainted with the successful use of the sex hormones together with guarding thyroid extract or iodine. There seems to be a general belief that *each* gland is specific for diseases of that organ. Some drug firms foster this belief.

Returning to the fatty acids, and unsaturated substances, as *fed*, we should consider the work of Rowntree and associates. These investigators fed an extract from wheat germ oil and caused experimental cancer in rats. The preparation was made by ether extraction, and it is well known that ether will dissolve fats and fatty acids perfectly. The small amounts of iodine in wheat germ would *volatilize* away with the solvent and leave the unsaturated fatty acids to cause profound overactivity and subsequent speedy exhaustion of the glands of internal secretion.

It is obvious that unsaturated substances are needed to balance against iodine, but that the best combination in many diseases, including sterility, rickets, and cancer, is to include *iodine* with the fatty acids, as in natural cod liver oil. A few clinicians have used cod liver

oil in cancer after irradiation. It is extremely valuable with added iron.

Similarly, when the seeds have lost their coats, as in polished rice, the iodine and other mineral elements are not present to keep glandular balance. It is thus that we see *de-coated* and thus unsaturated carbohydrates and fatty acids of rice and of other cereals by their demand for iodine causing overactivity of the glands, and finally, through liberated body iodine, hastening the breakdown of nerve sheaths. Nerves are covered by phospholipids, attacked readily by excessive amounts of iodine circulating in the body fluids, under a condition such that iodine-lacking starches and fats of seed constitute much of the diet. Our explanation of signs of glandular disturbance, iodine action, and Vitamin B₁ deficiency is the only one that answers the question as to why Vitamin B₁ is able to facilitate such rapid restoration in nerve function after apparent degeneration. The Vitamin B₁ stabilizes the endocrines and hastens the phospholipid return to the nerves. (See Vitamin B₁, page 81.)

It is with small, optimum amounts of iodine that cells and growth-acids are able to grow *unrestrictedly* and eventually to become *cancerous*. When the iodine which is ordinarily able to prevent such wild growths is reduced in proportion, because unsaturated substances have been applied to the skin, abnormal growth results. When there is vitamin deficiency, and the glands have been first overactive and then exhausted, the *iodine* is reduced in the body fluids, and cancers grow faster or are implanted more readily. (See page 94.)

Normally the fatty acids, amino-acids, and lipoids are so beautifully balanced by liquefying elements, and distributed by the blood and lymph, that normal growth and repair are accomplished slowly. In cases where cancers have regressed, after fevers or glandular therapy, it is possible to link such cures with increased iodine.

Experimentally, iodine in small amounts accelerates growth of tissue cultures of cancers and of glands; and large amounts will cause slow growth and even regression.

"Watch narrowly the demonstration of a truth, its birth,
And you trace back the effluence to its spring."

—BROWNING

CHAPTER XIV

Recent Studies with Carcinogenic
Substances

The search for cancer-inducing substances that are normally found in the body continues to be one of the most important in the chemistry of cancer.

Following the discovery by Kennaway and associates that an aromatic hydrocarbon (1, 2, 5, 6-di-benzanthracene) was cancer inducing, they tested 140 compounds and identified 30 that were capable of inducing skin cancer in mice after a course of skin painting with them. Of the more than 45 chemical compounds which induce cancer in experimental animals, the majority are *hydrocarbons*. The formation of carcinogenic compounds from hydrocarbons, as well as from *sterols*, involves the process of *de-hydrogenation*. And this process occurs in the human body.

If these carcinogenic hydrocarbons are *not* hydrogenated, or if the endocrines are exhausted, and hypofunctional, so that iodine is not available, their cancer-growth stimulating properties remain.

Hyperthyroidism precedes the development of various cancers, including the ones attacking the male breasts after a period of unnatural functioning (gynecomastia). Thyroid hyperfunction may very well be involved in the continuous release from the liver and gall bladder of accumulated derivatives of the bile acids, which are *dehydrogenated*, and desaturated of iodine, and thus ready to absorb iodine if it were available in protective amounts. Dehydrogenations would favor the acceptance of one of the halogens, such as chlorine or iodine. As we have already pointed out, the saturation with iodine of several growth acids and unsaturated hydrocarbons causes their inactivation as cancer formers, and inhibits their growth properties.

The three most potent cancer-inducing agents are benzpyrene, methylcholanthrene, and cholanthrene. A single subcutaneous in-

jection of any of these hydrocarbons will produce in susceptible strains of mice almost 100% of sarcomas within 4 months after the injections. Benzpyrene has been isolated from coal-tar.

At Harvard University, Dr. L. F. Fieser has emphasized the fact that methyl-cholanthrene is secured by dehydrogenation of *bile acids*, desoxycholic acid and cholic acid. Since bile acids are also agents in the production of *gastric ulcers* in experimental animals, we have potentialities in cancer formation that arouse concern about the chemical condition of the bile. Adequate iodine in the body may render *bile* cancer preventing.

Hall and Franks have reported that repeated injections subcutaneously of relatively large doses of *acetylcholine* produced osteo-sarcoma in experimental animals. This discovery led to the expectation that other substances normally found in the human body may prove to be carcinogenic.

When Wieland prepared methyl-cholanthrene from the bile acid-desoxycholic acid, it was first thought that abnormal metabolism of bile acids might be the precursor of cancer.

Further investigations by Fieser and tests with compounds synthesized by him, made at the U. S. Public Health Service laboratories by Shear, indicate that the chemical structure of bile acids (5 carbon ring) is not necessary in order that the substance may induce cancer.

As Voegtlin reminds us (*Science*, July 15, 1938) either the biochemical synthesis of the *sterols* or the *bile acids* might be pathological, and cancer-inducing substances could result. "The tissues can accomplish with ease chemical transformations which present day chemistry has failed to perform in the test-tube."

Schmid (1937) was able to induce epithelial tumors of the walls of the gall bladders in pigeons after a year of treatment by placing in them a solution of irradiated *ergosterol* in linseed oil.

We know that *cholesterol* accumulations appear in the form of gallstones, and also of lens cataracts, in animals that have been on vitamin-deficient diets. Thyroid overactivity, which marks the early stages of Vitamin A deficiency, furnishes the proper condition for the action of bile acids in producing gastric ulcer. Thyroid exhaustion which permits gallstones to develop would favor the accumulation of degradation products of the bile acids, which we know to be cancer inducing.

It is evident that normalization of the intake of iodine and the normal functioning of the iodine reservoirs will induce a great measure of protection against sterol-induced diseases, and will insure the prevention of gastric ulcers (due to hyperthyroidism) and stop liberation of dehydrogenated or desaturated bile acid derivatives which might be the seeds for distant or even liver cancers.

Instead of producing gastric ulcers by the application of irritants to the mucosa, Stewart and Lorentz (*J. National Cancer Inst.*, 3, 175, Oct. 1942) have introduced three well-known carcinogenic substances into the walls of the pyloric (glandular) region of the stomach in male and female mice. They used as vehicles mineral oil, lard, serum, and cotton thread, and introduced methylcholanthrene, benzpyrene, and dibenzanthracene. Adenoma, adeno-carcinoma, and sarcoma were thus produced. Adeno-carcinoma extended through the muscular layers and grew in the peritoneum. Transplanted to mice of the same strain by subcutaneous injections, one of the adeno-carcinomas has reached the twelfth generation. In these cases, there was no attempt to administer protective foods or drugs.

Hammett and Reimann (Lankenau Hospital, Philadelphia and Marine Station, Truro, Mass.) have shown that methyl-cholanthrene and dibenzanthracene stimulate new growth in the marine hydroid, *Obelia geniculata*.

Dibenzanthracene and other cancer-inducing hydrocarbons will produce tumors when painted on the skin. They will also cause sarcomas if injected subcutaneously, or cause malignancy of internal organs of mice. There seems to be a general *systemic* disturbance induced by many carcinogenic agents which have local effects as well.

Chemically induced tumors are not limited to the tissues where these carcinogenic agents are injected. Andervont has been able to produce lung cancers in mice with no signs of tumors at the point of subcutaneous injections. Strong succeeded in producing mammary cancer in mice by applying methyl-cholanthrene to the skin of the back.

Voegtlin and associates (Nat. Cancer Inst.) have found that if methyl-cholanthrene was painted on the skin of mice fed a diet rich in sulphur, they developed leukemia. On low sulphur diet, the methyl-cholanthrene treatment resulted in arteriosclerosis.

PROTECTIVE AND CURATIVE MEASURES

Hydrogenation (and thus saturation) of shale oils has been successfully instituted in Britain for some years, and the "shale-oil cancer" of workers in mills, where oils splashed on them, has been sharply reduced.

Saturation (with chlorine or iodine) or *hydrogenation* of the shale-oil derivatives causes their inactivation so far as the skin cancer is concerned. Similarly, injurious effects of amino-acids, fatty acids and lipoids *may* be prevented by adequately functioning glands. Some of the facts about which we have experimental evidence have not been specifically applied to the cancer problem, though known to nutritionists, biochemists and endocrine workers.

Dr. Fieser has studied the kidney excretions of rabbits that proved resistant to methyl-cholanthrene, and isolated certain substances which showed a chemical relationship to prothrombin. Vitamin K is the substance that facilitates the formation of prothrombin, necessary for proper blood clotting. It is hoped that Vitamin K may protect animals from the development of cancer by maintaining prothrombin at a high level, sufficient to inhibit hydrocarbon carcinogenesis. Endocrines that control calcium and iodine are here involved, for they are concerned with the clotting of blood.

Reimann was able to delay the development of skin tumors in mice by combining parathiocresol with *dibenzanthracene*, which, unguarded, produces cancer when applied to their skin. Thiocresol is used to stimulate cell proliferation in the healing of superficial wounds.

Haddow found that carcinogenic hydrocarbons injected daily in small doses were able to inhibit the growth of transplanted tumors in rats. This is in line with the stimulating action of small amounts of unsaturated hydrocarbons on the endocrine glands and other storehouses of iodine.

CHAPTER XV

Mammary Cancer—An Example

"The best doctors in the world are Doctor Diet, Doctor Quiet,
and Doctor Merryman!"

—SWIFT

Since mammary cancer is so common, and there is a considerable body of experimental evidence as to its origin and treatment, we shall survey it, referring to appropriate sections of this book for extensive explanations.

OCCURRENCE

There are about 12,000 deaths from cancer of the breast annually in the United States. The greatest number of cases appear after the age of 45, especially after 50 and 60 years. Cancer of the breast is not uncommon after 30, and it may appear as early as the second decade.

Breast cancer is more frequently found in single than in married women; it develops more commonly in those women who have not *nursed* their babies than in those who have. In the Japanese women, who do not resort to artificial suckling of their babies, cancer of the breast is rare. The African natives suckle their infants for at least 18 months, the vast majority for 2 years, and are notably free from breast cancer.

Widows and divorcees have a higher death rate from mammary cancer than married women. This has been attributed to the influence of emotional tragedies on the circulation and the endocrines. Taylor's evidence on psychic factors will be mentioned later.

The early removal of lumps in the breast is advocated, in order to prevent them from becoming malignant. Microscopically, it is very difficult for the most expert pathologists to determine the character of borderline tumors. And delay to see if the lump will grow

may result in the rapid migration of metastases. The first small lumps are usually painless.

HEREDITY

Some of the most convincing proofs of inheritance of a tendency to develop cancer have been gathered by Mrs. Macklin, of London, Canada. We have elsewhere given a general discussion of the subject, but a few supplemental instances will illustrate the matter of glandular involvement.

In Horsley's cases, three patients were sisters; all had cancer of the breast tissue, misplaced in the armpit. Inheritance of a tendency to form accessory breast tissue in the axilla was combined with inherited tendency to cancer of that tissue.

In another series of cases, Leschoziner reported a mother and 3 daughters all of whom died before the age of 22 with breast cancer.

Power cited the most remarkable family of all, for breast cancer appeared in the father, 2 sons, and 6 daughters.

It behooves any person with cancerous inheritance to be ever watchful, but *not* fearful.

Since 1907, the author has benefited by association with the most distinguished scientists of the world, at the Marine Biological Laboratory, Woods Hole, Mass.

In presenting various portions of the MS for criticism we had the opportunity to see the section on "Cancer, the Genetic Aspects" which will appear in the enormously valuable book by Dr. R. Ruggles Gates, "Human Genetics." Dr. Gates, who is Emeritus Professor in Botany, University of London, F.R.S., F.L.S., and medallist of various societies here and in Europe, has inspected the chapter on Heredity here presented, adding to its clarity.

Dr. Gates directed our attention to his discussion of McDonald's work, which seems to fit exactly into our own thesis.

"McDonald (1942) suggests that the low cancer rate in such native races as the American Indian, the African negro, and the Eskimos is because their meat diet consists less of muscle and more largely of viscera, the latter containing a cancer-inhibiting substance." WE have shown why the viscera will bring iodine and other essential elements to induce cancer regressions.

Murphy and Goldstein (1940) show that about 1 in 59 children born to mothers following *irradiations* had anomalies. Dr. R. R. Gates ("Human Genetics") stresses the danger from this source, for such anomalies are likely to be inherited.

Bainbridge, whose 1939 paper on heredity and cancer has had wide distribution (see page 31), says, "There is strong reason to believe that the individual risk of cancer can be diminished by the eradication, where such exist, of certain conditions which have come to be regarded as predisposing factors in its production." Medical directors of insurance companies do not consider the possible inheritance of a cancer tendency in granting a policy, or in the size of the premium for any given age.

In his letter to Dr. Bainbridge, Director C. C. Little, Secretary of the American Society for the Control of Cancer, said, "It is perfectly fair to state that there is no experimental evidence from human material or from other very much related to it that would lead one to believe that heredity is a factor of prime importance in determining the incidence of cancer."

It would be very illuminating, and perhaps encouraging, if we could identify an inherited tendency towards goiter in human families where cancer was also prevalent. For goiter-susceptible families have been able to prevent its development by diet and iodine therapy.

OCCCLUSION OF DUCTS, TRAUMA

In 1922 Yamagawa, by injecting coal-tar and lanoline (sheepswool fat) into the mammary ducts of mice, was able to induce the development of tumors.

Bagg, in 1924, stimulated to experimentation by the clinical reports of James Ewing, produced in rats artificial stagnation of the mammary glands and resultant experimental cancer. He ligated the terminal ducts to the nipples on one side of the body in breeding females, and then permitted them to bear young. The young were suckled on the unoperated side. In 87% of his animals breast tumors developed. The controls had only a 5% tumor incidence. This experiment links with the evidence from cases of mastitis, of blows, and of *failure to nurse the infants*.

While breast injuries are much more common in men than in women (3 to 1), cancer of the breast is in the proportion of 116 in women to 1 in men. The breasts of a woman are more protuberant, and thus susceptible to blows. And we must not forget that devices used to support the female breasts may be irritating. Crude and rough surgeons may be guilty of such manipulation of breast tumors that they cause metastases.

In 1925 Bagg and F. E. Adair studied the milk histories of 200 mothers and found that in only 9% was lactation carried to its complete issue. It is well known among veterinarians that cows milked regularly have in only rare instances cancer of the udder. On the other hand, bitches from whom puppies are withdrawn early are likely to become cancerous. Our earliest evidence as to the effects of ovariectomy on regression of breast cancers came from the reports of veterinarians after spaying dogs.

In a recent survey of the British report on cancer it has been shown by S. Peller (1940) that cancer of the breast is rare among the wives of unskilled laborers, who ordinarily nurse their babies; but that professional women, who are accustomed to early weaning, have breast cancer more commonly. Spinsters over 54 had the highest rate. This could be related also to glandular insufficiency that caused them to remain unmarried. (See Glandular disorder, page 165.)

MASTITIS

Taylor, in his paper discussing 261 cases of mastitis, has given us a convincing picture of the relationship of this inflammatory condition to breast cancer. And Montrose Burrows, in his 1931 report, cited 180 cases of breast cancer in St. Louis, where a previous chronic mastitis had occurred. He says, "In this investigation, I was impressed by the similarity in histology (microscopic anatomy) of the precancerous breast lesions to thyroid goiters."

CERVICITIS

In 114 cases, Taylor secured histories of infected lacerations of the cervix, which is the neck of the uterus. Here he concludes that the pelvic inflammation may have its effect on the circulation, and

thus on the breasts. It is not unreasonable to link with this a disturbed sex cycle, so ably discussed by Ingleby. (See page 123.)

REMOVAL OF THE UTERUS

Operative removal of the cervix of the uterus has been reported to induce a cure of breast cancer. On the other hand Taylor has described 11 instances of breast cancer that followed the removal of the uterus. And Aschner maintains that a *special tendency to cancer* exists in the breasts of women who have had the uterus removed. It is possible that the pelvic plexus of sympathetic nerves and the circulatory system may be so affected by such an operation that glandular imbalance is set up. Again, the retained ovaries might exert their influence, when the sex cycle was thus stopped.

BAD TEETH, POOR NUTRITION

The distinguished physician, Oliver Osborne, of Yale, has written a book in which he describes the interrelationship between the teeth and the glands, especially the thyroid. Not only do infected teeth influence the health of adults, but in the case of pregnant women the development of their babies may be affected, through action on the glands of internal secretion of the mother.

Many cases of degenerated or abscessed teeth have been cited by clinicians in connection with cancer of the skin and the breasts. As Burrows has indicated, mammary glands are developed from skin glands. Burrows has linked diseased teeth with lowered resistance of the body to precancerous lesions. And he has noted that in some cases the removal of only one tumor and of diseased teeth was followed by the disappearance of other tumors in the same person without further treatment. Bainbridge and Lane have reported the disappearance of lumps in the breasts, when patients merely had diseased teeth removed. Glandular defense against infections was robbing the body of cancer-destroying substances.

The nutrition of patients may be adequate, except for the lowered ability to use their food, caused by infected teeth. We shall have occasion to consider diet later. (See also Nutrition, pages 50-67.)

INTESTINAL STASIS

Leonard Williams, quoted by Dr. W. S. Bainbridge in his article on "Intestinal toxemia" (*Med. Jour. and Rec.*, 1925), has said, "There are hundreds of people who have a daily evacuation of the bowels, but who are nevertheless walking septic tanks. These tanks are terrible depressors of the thyroid, and unless you empty and disinfect them, your correct diagnosis of thyroid inadequacy and its logical thyroid therapy will avail you nothing."

Bainbridge has recorded numerous cases where surgical correction of intestinal stasis causes the regression of breast tumors which could well be considered precancerous. He has been able to cause the disappearance of lumps in the breasts by proper eliminative medication and endocrine (thyroid) therapy, without operation. He is careful also to institute support for dependent breasts. Bainbridge has described to the writer many cases from his own practice, and has also cited the evidence of Sir Arbuthnot Lane, where breast tumors regressed after relief of intestinal toxemias.

The writer believes that by such surgery and medication the iodine which accumulations of feces had previously bound to their amino-acids and fatty acids is made available for effective action. Skatol and indol, which are putrefactive protein derivatives, will seize needed iodine, and cause derangement of the thyroid gland. The normal liver continually desaturates substances, sending iodine into the *bile* and intestines. We have previously discussed the fact that the "old" Eskimos ate foods in which the iodine protected them against protein putrefaction, thyroid disturbance, and cancer (page 55).

CYCLIC DERANGEMENT

In 1932 Ingleby of Philadelphia demonstrated that premenstrual proliferation is extremely rapid in the breasts of women, from the middle ten days of the cycle up to a day or two before the onset of the menstrual flow. Tumors increase in size up to that time. Then they regress in size very rapidly. Scheringer has shown that at the onset of menstruation the *iodine* content of the blood increases up to 25% greater than before menstruation. And Spiegler found that

potassium gradually increases in the blood during the premenstrual period.

The gradual increase in size of the incipient tumors may be attributed to the deposition of amino-acids, sterols, fatty acids, and hydrocarbons derived from bile acids, which are transported through the blood by liquefying elements, including potassium and iodine. These accretions are *rapidly broken down* at the *onset* of the menstrual period when the maximum concentration of both *potassium* and *iodine* in the blood has been reached. Whether metastases from the breast tumors are at this time distributed to the axillary lymph glands, the lungs, the vertebrae, or other points will depend in part upon the amount of *calcium* that may be mobilized. A marked rise in calcium normally occurs in the blood at the menstrual period, for then the thyroid is hyperactive. Hyperthyroidism may cause as much as 250% increase in the blood-calcium (Aub). A thyroid which has been previously overactivated, and then becomes exhausted, cannot aid in mobilizing either iodine or calcium. Calcium will retard metastases and dehydrate the tumor.

Dr. Ingleby in experiments with female rats was able, by disturbing the *sex cycle*, to induce cystic condition in their breasts. Menstrual abnormalities occurred in 82 patients at the same time that breast symptoms arose (Taylor).

GLANDULAR DISORDERS

As a precursor of cancer of the breast in males, there may occur an abnormal overactivity of the thyroid gland. The breasts of men may be greatly enlarged, and even secrete milk. Such a condition, known as "gynecomastia," was noted in association with hyperthyroidism by Von Basedow, the goiter specialist, in 1848. Numerous other clinicians have since recorded it.

Prostate gland removal may be followed by hyperthyroidism, gynecomastia, and later by *cancer* of the male breasts. Moreover, there are reports that about 25% of hermaphroditic individuals are tumorous. Sex gland insufficiency is certainly related to cancer growth in some cases.

The *female sex hormone*, originally secured from the ovaries, but now derived from pregnancy urine, and in largest amounts from the

urine of *stallions*, has been used in experiments on rodents to cause cancer of the breasts. *Folliculin*, *theelin*, and *estrin* are all terms used to designate the sex hormone, supposed to be female.

Folliculin has been used to induce lactation in male guinea-pigs, rats, and mice. It was also used some years ago to produce a change of plumage in castrated roosters to the feathering and coloration of hens. But such a hen feathering was also produced by thyroid extract in castrated cockerels.

The most striking experiments with folliculin were those first recorded by Lacassagne, who in 1932 was able to induce mammary cancer in young male mice by regular injections of folliculin, which began at the age of one week.

Multiple transplants of the anterior pituitary gland cause breast cancer in mice. Murray was able in 1928 to produce mammary cancer in male mice by transplants of the ovaries. There is quite evidently a cleancut relationship between glandular function and the development of cancers. Thyroid extract in heavy doses will not seriously affect individuals if the doses are widely separated. But Kendall showed that small, repeated doses of thyroid extract will cause a goiter. Eventually overactivity of the thyroid may cause serious chemical imbalance, paving the way for disease.

Folliculin is known to cause a rise in basal metabolism. It has been used to induce goiter in rabbits. Cyclic overactivity of the thyroid gland is associated with menstruation and the heat periods of animals, as is well known.

In 1916, Loeb first showed that, in strains of mice with high incidence of breast cancer, females that were ovariectomized (spayed) before they were six months of age showed a marked decrease in tumor incidence. Cori, in 1927, reduced effective ovariectomy to 22 days, and entirely prevented mammary cancers in cancerous strains. Murray has shown that virgin females of strains in which breeding females have breast cancer are not so likely to have it.

In tests with folliculin, Cramer and Horning of England found that the whole system of glands of internal secretion was affected after the use of *pure* folliculin. They compared the general condition to that secured by removal of the *pituitary gland*. There was an arrest in growth and atrophy of the adrenal glands and the testes of male

animals, loss of hair, and general debility, if the pure folliculin was used. And cancer of the breasts followed. In 1931, Louis Berman directed attention to the fact that cancerous patients frequently resemble those with acromegaly, which we have long known to be related to pituitary disease.

Basing their experiments on the evident influence of the pituitary gland, in opposition to such changes, Cramer and Horning in 1938 used the thyrotropic hormone of the pituitary gland to prevent such conditions, including breast cancer. The thyrotropic hormone of the anterior pituitary has profound effects on the thyroid gland, and it has been used to induce tadpole metamorphosis, a test for iodine.

With evidence definitely furnished that the "sex hormone" cannot be used safely in the treatment of premature menopause in women without danger of inducing cancer, it is gratifying to learn that at our suggestion some clinicians now use thyroid extract or iodine in conjunction with "theelin" and "folliculin."

As a treatment for cancer of the breast, thyroid extract has been in use for some 40 years. The idea of specificity of glands caused some physicians to use mammary extract. Others, who were more nearly right than has been realized, used a combination of thyroid and ovarian extracts, containing all their protein, fats, lipoids and minerals.

It seems much more logical to use iodine or thyroid extract than to mutilate a woman by removal of her ovaries, a practice which will cause speedy derangement of the whole endocrine mechanism, with heavy losses of fats, vitamins, calcium, iron and iodine. Even normal menopause is associated with hyperthyroidism. To add further insults to the body by administering "sex hormones" that consist of unsaturated *hydrocarbons*, known to be cancer inducing, is unwarranted.

The *complete* ovarian extracts, in use many years ago, and even now valued highly by keen clinicians, contain in proper balance essential minerals, cholesterol, fats and unsaturated fatty acids—as in lecithin. They are rich in iodine, but it is in *balance* with fatty acids and sterols.

Parabiosis, in which a male and a female rat, placed side by side, have their blood vessels joined, was shown by Biedl, in 1927, to cause the sexual cycle of the females to cease, until the union of blood vessels was severed. Murray stopped the development of cancer in female mice by similar technique. But thyroid extract and anterior pituitary injections also stop the sex cycle in experimental animals. They have been successfully used to treat breast cancer.

SURGERY

Surgical intervention in human breast cancer was conducted with great skill and thoroughness in the 17th century by Fabricius Hildanus. This brilliant pioneer executed *complete* operations and dissected out the metastatic masses that had extended to the axillary lymph nodes. Such a procedure has been adopted by the most successful surgeons, and there are many records of long-standing cures. The "Cured-Cancer-Club" consists of women who have survived operations of this type, where sane surgeons did not hesitate to do the necessary complete job. Surgery is not so spectacular as radiation, but it has elements of certainty and less risks of metastatic dispersal.

Tinker in his surgery of *malignant goiter* (*Archiv. Surg.*, 1933, 26, 705-711) uses electro-surgery and gentle handling to prevent the dissemination of metastases. He cites the caution of Clute and Smith (1929) against biopsies of potentially malignant adenomatous nodules of the thyroid, "because of the ease with which these tumors gain access to the blood stream." Roughly executed examinations of the *breasts* are too frequent, surgeons state.

Tinker says, "If radio-cutting were used the danger would most certainly be avoided; medium or slow cutting currents almost certainly seal the blood vessels and lymphatics."

Barthels (1931) cited 86 cases of authors who reported one or more cases of apparently benign goiters which metastasized and caused death. Thyroid metastases are most likely, according to Cohnheim (1876), to occur from the thyroid to flat bones. Thyroid cancers are disseminated to the breasts in many cases. To what extent electro-surgery is now in use in *breast cancer* is not known to this writer.

The time factor is of greatest importance, for all too many cases of cancer do not reach the surgeon until they are in an inoperable and hopeless condition. Fortunately the Woman's Field Army of the American Society for the Control of Cancer has done a truly wonderful job in publicizing facts about cancer, and urging early visits for diagnosis and treatment. New York State reports in 1941 showed a reduction in cancer mortality among women, aged 25 to 44 years, in whom a decrease of 10% occurred from 1930 to 1940. Cancers of the breast and of the uterus are the most frequent forms of cancer in women.

Lane-Clayton has told us that if breast cancer is operated in the *early stages*, and is complete enough to include the glands in the armpit, 90% of the patients will survive after ten years. If the growth has been allowed to extend beyond the breast region before operation, 90% of the cases will be dead at the end of the ten year period.

Breast cancer may appear in women as young as 20, and it is dangerous at any age, but growths in the breast after 50 are in a large percentage of cases likely to become malignant very rapidly. Bloodgood has urged that at such an age a *delay beyond one month* after first signs of a lump appear is likely to prove a fatal postponement.

Clinicians have reported that operative removal of the gall bladder, the uterus, the thyroid gland or the ovaries may cause regression of breast tumors, and lumps. As we have pointed out, uterine operations and thyroid operations may *favor* the development of such growths. Supplemental treatment is indicated in either case, and has been adopted quite regularly where the ovaries were removed. (See page 170 for *thyroid medication* after ovariectomy.)

RADIATION

There is great difference of opinion among the experts with regard to supplemental X-ray and radium treatment of breast cancers. One school, fearing metastatic dispersal of fragments by radiant energy, opposes *any form* of irradiation before the operation, but uses it to "clean up" masses of wild cells that have escaped the knife.

The other group favors preoperative or postoperative radiations as safety measures. Unfortunately many cases of breast cancer come to the surgeons too late to hope for cure by removal of the breast and axillary glands.

Sir John Fraser considers preoperative deep irradiation of the breasts to be harmful. Dr. Frank E. Adair of the Memorial Hospital, New York, in his article on surgery and irradiation in breast cancer (*J. of the Am. Med. Assoc.*, Feb. 20, 1943, vol. 121, pp. 553-558) is most emphatic in urging immediate surgery, with no preoperative irradiation. He points out the fact that preoperative irradiation may cause a delay of three months before needed surgical intervention can occur, and he stresses the danger coming from *irradiation* itself. He favors postoperative irradiation by the modern divided dose method.

Irradiations of the ovaries and of the thyroid gland have both been reported to cause regression of metastatic nodules in the breasts. Such irradiations make available activated elements, with *carcinolytic* power.

GLANDULAR THERAPY

Extracts from all of the glands of internal secretion have been used in breast cancer with reputed success. (See pages 155-188.)

ASCITIC FLUID

In 1910, Hodenpyl secured ascitic fluid drawn off from a patient with breast cancer, tested it with experimental animals, and then used it successfully to improve the condition of 47 human cases. He injected the fluid into the tumors, or the veins. In 1913, Lewin described a similar case, in which he withdrew fluid from a case of carcinoma of the breast and injected it subcutaneously. At the end of 18 months the patient was cured.

In mastitis (inflammation of the breast) a number of physicians have been able to use the accumulated fluid as a source of curative injections. This it seems is taking advantage of the defensive chemicals which, in the center of a growth, cannot break down the wild cells. Fluids from the chick (Rous) sarcomas have also been used

to cause their regression. (See page —.) Iodine inactivates the Rous chick sarcoma (Mellanby, 1938).

OTHER CHEMICAL ATTACKS

At the Wistar Institute, Philadelphia, Corporal I. Cornman reported (1944) the selective action of penicillin on sarcoma cells in rats and mice. A few cancer cells were killed and normal cells were left unharmed. It required 3 times the dose for cancer cell destruction to hurt the normal cells.

Untreated cells gave cancer to all the controls, and penicillin-treated cancer cells were ineffective when transplanted to cancer-susceptible rats. Wistar Institute cancer workers await further studies by Cornman and others.

Yeast, starch, chlorides, iodides, colchicine, distilled water, and heptyl aldehyde (derived from oil of wintergreen) have all been successfully used in experimental mammary cancers in animals. Transplanted tumors will in many cases regress "spontaneously" in a short time. This fact has led to the feeling among clinicians that studies with mouse cancer neither prove nor disprove results obtained with human cases. Some experimentalists or reviewers use a very small number of animals to furnish material for an iconoclastic article. On paper they may concur, or disagree violently, with other workers. When the evidence becomes overwhelming, these persons then "knew it all the time."

The motto of pseudoscience is that of the car manufacturers, "When better —s are made, *we'll* make them." In the meantime even the best endowed laboratories sometimes follow blind leads, and ignore facts that have not emanated from their own staff. Human antagonisms and jealousies retard all progress.

Just how cancer workers can deny the relationship of diet to cancer when evidence as to the transformation of a goiter to thyroid cancer is so cleancut we cannot see. It is easier to consider the "thyreotropic hormone of the anterior pituitary" as a mystery than it is to admit the iodine content of that gland and the action of iodine on the *lumps* that are so easily broken down by veterinarians.

When the greatest radiologists finally agree that irradiation of *any* cancer will activate its iodine, just as the iodine of a thyroid

cancer is made more carcinolytic, it will be a *new* discovery. But the 15 year record of a quiet, efficient radiologist is known to others through this writer. (See page 143.)

DIET AND BREAST CANCERS

At some length we have taken up the subject of nutrition and the origin and treatment of cancer (pages —). Our summary at this time will merely emphasize a few points.

Intestinal stasis has been linked with the development of lumps in the breast and its relief with their disappearance. The close relationship between an adequate diet and the condition of the thyroid gland is obvious when we realize that vitamin-deficiency diseases are all related to the thyroid and the other endocrines as well.

A plentiful supply of natural raw fruits and vegetables should accompany a well-balanced diet of animal and vegetable foods. To insure adequate *minerals*, the marine foods should be included regularly. In cases that have been radiated, there is especial need for such foods as the dark meat of mackerel, tuna, and other marine fish rich in iron, calcium, and iodine. Supplemental calcium, well balanced, may be secured by hot or cold clam juice, which is extremely pleasant as a mid-morning or mid-afternoon lunch. Dairy products furnish easily digestible *fats*, which aid in normalizing the glands. Vitamin concentrates should not be necessary, and may be injurious.

For some years clinicians have used cod liver oil plus iron in radiant energy sickness. (See page 79.) This method is beneficial in the anemia of cancer cases, and furnishes iron, iodine and calcium, with the easily digestible fatty material which aids to normalize glandular function.

Short fasts, by insuring the absence of fats, carbohydrates, proteins, and lipoids which interfere with the circulation of beneficial elements, may be very valuable, but should never be undertaken without adequate medical supervision in cancer cases.

Limited diets such as grape juice, bananas, fruits of other kinds, have had their champions, and if indulged in for short periods may be quite beneficial. But here again fads are dangerous, as a cancer patient is in many cases not strong enough to withstand such body-deranging limitations in essentials.

WORRY AND BREAST CANCERS

The psychic factor in breast disease has been considered by Taylor to an illuminating extent. He points out that in many instances breast symptoms were made worse during periods of anxiety, resulting from economic worries, illness of relatives, or marital difficulties. Since Taylor and Montrose Burrows had many cases in which definite thyroid enlargement was associated with breast cancer, the mental state was beyond a doubt influential in such cases to an unusual degree. "Thyroid nervousness" might interfere with the normal circulation of blood to breasts. We are thus introduced to the final section in our present series.

"What need is there of suspicious fear, since it is in thy power to inquire what ought to be done? If thou dost not see clear, stop and take the best advisors."

—MARCUS AURELIUS ANTONINUS

CHAPTER XVI

Mental States and the Development and
Cure of Cancer

A short time ago a woman said to me, "If I thought that I had cancer, I should just curl up and die." She had been talking about the number of her friends who had gone through the agony of cancer, after delaying treatment until too late. The attitude of fear is quite general today, because so many persons live only a short time after cancer diagnosis has been made. The author hopes that this book will send persons to their physicians for frequent check-ups on health.

French clinicians, noting the great increase in cancer after the World War of 1914-1918, said, "Emotional strain, by its action on the sympathetic nervous system, seems to predispose to cancer."

Sir Lenthal Cheatele in 1905 suggested that a definite relation existed between the incidence and the spread of cancer and the *nerve supply* of the areas involved. He recorded cases of cancer in anesthetic areas of the skin in support of this thesis.

H. Snow has linked cancer of the uterus and cancer of the breasts with worry, and inquires if many cases of such cancer are not due to the neurotic state. He quotes Dr. Walshe, who observed similarly in 1848, stating, "It would be vain to deny that facts of a very convincing character in respect to the agency of mind in the production of this disease are frequently observed."

Held in 1924 said, "That the mental attitude of a patient has much to do with the progress or even development of carcinoma after the patient has been scared into the cancer mentality by careless or tactless attendants is undoubtedly true. Fear, grief, worry, shock are well known to influence secretions."

Cancer phobia is general. And it has been shown that during emotional disturbance blood iodine is increased from 20% to 50% in human subjects. This means that the impact of worry and fear

on the glands of internal secretion has caused them to become over-active.

Doctor G. W. Crile stated quite clearly at the World's Fair program of the American College of Surgeons that, by the proper exercise of reason, the "diseases of civilization" may be warded off.

Doctor Crile showed that the brain and the thyroid gland supply man with his power of sustained energy and activity, mental, emotional and physical. "The adrenal-sympathetic system, which in turn is maintained at a constant level of activity by the thyroid gland and is given its outbursts of energy by the brain, is the most active in the expression of emotions. This group of executive organs is primarily responsible for the state of civilized man."

The brain may maintain too high a state of activity, and a nervous breakdown may result; or when the thyroid runs wild, exophthalmic goiter develops. Even if the brain and the thyroid do not show injury, some weaker organ of the "kinetic system" may give way. Dr. Crile lists diabetes, certain types of heart disease, and stomach ulcers as thus likely to occur through the high speed of civilization.

"Man cannot lessen his brain capacity, he cannot lessen his glandular power, but he has at his disposal the use of the finest tool civilization has wrought, namely, his reason. The civilized fraction of man should be able to control the wild reactions inherited from his long past."

In his report in July, 1940, on the statistics compiled by a recent British summary on cancer, Peller has cited the much more frequent deaths of widows and divorcees from breast and genital-organ cancer than among married women. The death of a husband is an emotional tragedy and influences the glandular mechanism of the age group affected, between 35 and 54. An unsatisfactory marriage, leading to a divorce, may be a *cause* of the cancer, or it may be an effect. For extremely important glandular derangements pave the way for cancer, and such glandular upsets could make the wife an incompatible person. It should also be pointed out that certain contraceptive measures are known to cause cancer of the uterus. Divorces are likely to come in families where there are no children.

Gastric ulcers may pave the way for gastric cancers. In his book on "Worry and Disease," Podolsky mentions the case of a woman

of 38 who for more than a year complained of a persistent pain in her stomach and intestines. Her mother, father, and one brother had died of cancer, and she feared that she too had cancer. When reassured by a complete and thorough examination, her condition improved. But by continued worry, such a person might cause the selfsame thyroid disturbance that has been shown experimentally to favor gastric ulcers in animals.

Specialists on gastric ulcer have emphasized the fact that fear and worry are common causes in man, and hence experiments with animals are not completely successful in elucidating certain problems.

We do know that lack of fats and of the fat-soluble vitamins is responsible in animals as in man. And we know that the Sippy diet, rich in milk and cream, is curative.

Hyperthyroidism is associated with the development of ulcers caused by dietary deficiency, and it is also the result of profound mental disturbance which causes iodine to be liberated in large amounts from the midbrain and the pituitary.

A well-known cancer hospital head most pessimistically stated four years ago, in a syndicated news article, that efforts to aid cancer patients by *diet and medicines* which were made by general practitioners after the sufferers had been given up as hopeless by specialists were futile.

He said that in cases where surgery and radiant energy had failed to cure or even to benefit, the supportive treatment given by the home physicians sometimes "appeared to benefit them." But, said he, "the improvement is only temporary, and is due to mental suggestion, for the patients die, eventually—*of cancer.*" *

This statement was sincerely made by a man who was apparently in complete ignorance of the remarkable discoveries of the past 50 years with regard to the effects of the mind on the glands of internal secretion, and thus upon the whole physiological mechanism. He was also innocent of any knowledge of the supportive diets and medication that are indicated in anemias, pregnancy, and cancer.

* This cynical pronouncement reminds us of the pompous physician who was asked by the tearful wife if he was *sure* that her husband had pneumonia. He replied, "Madam, when I treat a patient for *pneumonia*, he *dies—of pneumonia.*"

While the majority of able cancer specialists realize the importance of inducing the proper mental condition in their patients, few of them have been as forthright as Doctor N. Treves of the Memorial Hospital, New York City. In his address to the Medical Society of the State of New York (May 11, 1944) Dr. Treves said:

"When a patient knows that he has a cancer, it seems most desirable to hold out the hope of recovery even to the last. The different mental outlook of a man who believes his condition to be absolutely hopeless from that of a patient who believes that he has even a 1 to 1000 chance of recovery is enormous.

"Many patients who will ask to be told the worst are the least fitted to know it."

Dr. Treves referred to the occasional "spontaneous" or natural recovery of some patients, as reported in several hundred cases. He said, "Even against hopeless odds, one may most infrequently expect regression and even disappearance of an advanced cancer." Perhaps certain cancer cures have made their reputation after such regressions. It is certain that dietary and medicinal supportive treatment will bring up the morale of patients, while others may keenly recognize that they are sent home to die and "decrease the surplus population."

Radiologists and surgeons have been slow to accept evidence of the value of some supportive medicinal and dietary regimes. A notable instance of a surgeon-radiologist who has availed himself of new discoveries is Dr. D. T. Quigley. Dr. Quigley, as a result of data secured from 2707 patients having tumors and cancers, found that nearly all were afflicted not only with some form of benign or malignant tumor, but with other diseases, including gall bladder disease, heart disease, arteriosclerosis, and ulcers of the digestive tract. *Multiple vitamin deficiencies* were present and the vitamin intake had been low.

Dr. Quigley has used "appropriate dietary treatment" in pre-cancerous and cancerous cases with excellent results. He supplies vitamins, calcium, iodine, and iron, in cancer, as in anemias.

Dietary and medicinal adjuncts to conservative surgery, and appropriate irradiations, will bring *hope* to many a fearful cancer patient. They will make available some of the needed foodstuffs of all

kinds, lost in the ravages of the disease, and even lacking for some years before cancer appeared.

The mental state is of incalculable importance in curing cancers. The great Doctor Alexis Carrel, after witnessing the actual regression of a cancer at Lourdes, was bound to accept the influence of faith. When we realize that prayer and faith will aid in slowing down glands that are overactive, and that calm hope will so conserve essential substances that some diabetes cases recover, we can see how the proper utilization of cancer-destroying elements is brought about by stabilization of the glands which control their distribution.

The purpose of this book will be fulfilled if readers go to their physicians for frequent check-ups, and thus enable experts to attack precancerous conditions in time, with the *hope* that statistics now present for speedy cure.

"At worst, I have performed my share of the task;
The rest is God's concern; mine merely this,
To know that I have obstinately held by my own work."

—R. BROWNING

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