

The conquest of cancer : a plan of campaign being an account of the principles and practice hitherto of the treatment of malignant growths by specific or cancrotoxic ferments / by C.W. Saleeby.

Contributors

Saleeby, C. W. 1878-1940.

Publication/Creation

New York : F.A. Stokes, 1907.

Persistent URL

<https://wellcomecollection.org/works/hqd25dz5>

License and attribution

This work has been identified as being free of known restrictions under copyright law, including all related and neighbouring rights and is being made available under the Creative Commons, Public Domain Mark.

You can copy, modify, distribute and perform the work, even for commercial purposes, without asking permission.

**wellcome
collection**

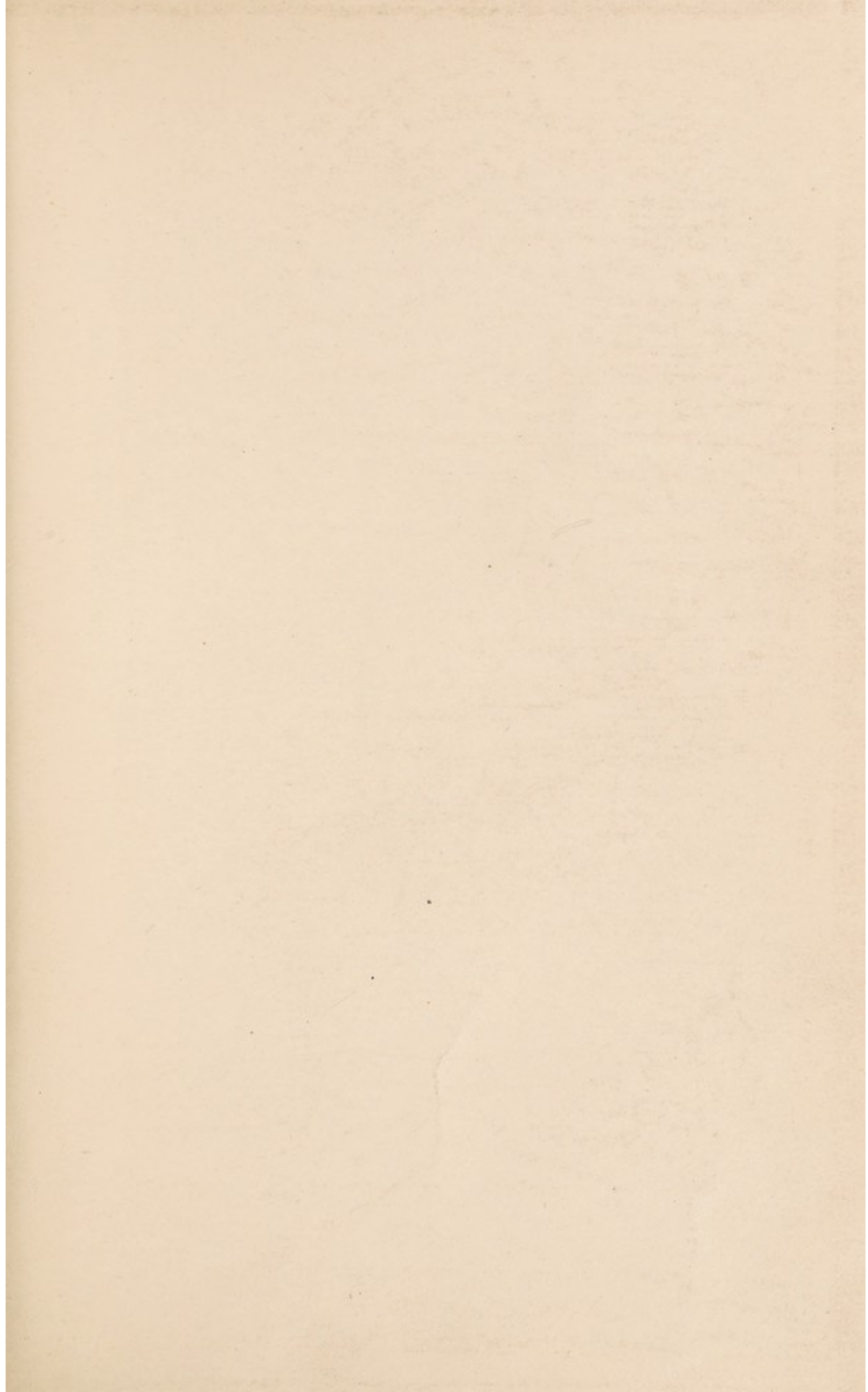
Wellcome Collection
183 Euston Road
London NW1 2BE UK
T +44 (0)20 7611 8722
E library@wellcomecollection.org
<https://wellcomecollection.org>

THE
CONQUEST OF
CANCER

Good



22102085809



ERRATA

p. 57, line 12, *for* 1899 *read* 1889

p. 73, *add note*—Since the earlier copies of this volume were struck off I have been made aware of much further evidence which suggests, apparently beyond question, that over-eating is a predisposing cause of cancer.

p. 83, *alter footnote to*—This paper appeared in the *New York Medical Record*, Oct. 19, 1907.

p. 100, delete footnote ³ and the numeral ³ at end of line 5

p. 159, *add to the text*—We see before us the dawn of a new era in therapeutics—the era of the control of vital processes (not of cancer alone) by ferments—at a date when chemistry is still unable to isolate a single ferment of any kind.

p. 213, delete third sentence in second paragraph, “But though . . . discussed,” put numeral ¹ at word *done*, line 9, and add footnote as follows:—

¹In the *Deutsche Medizinische Wochenschrift*, Sept. 19, 1907, Drs. Bergell and Sticker make a further report from the Berlin Institute of Cancer Research. In the words of Prof. Strauss, of the University of Berlin, they report “retrogressive metamorphosis in a sarcoma experimentally produced in a dog, by injection of this specific liver-ferment at a period when the question of spontaneous cure could no longer be entertained, and which finally resulted in the complete disappearance of the tumor.”

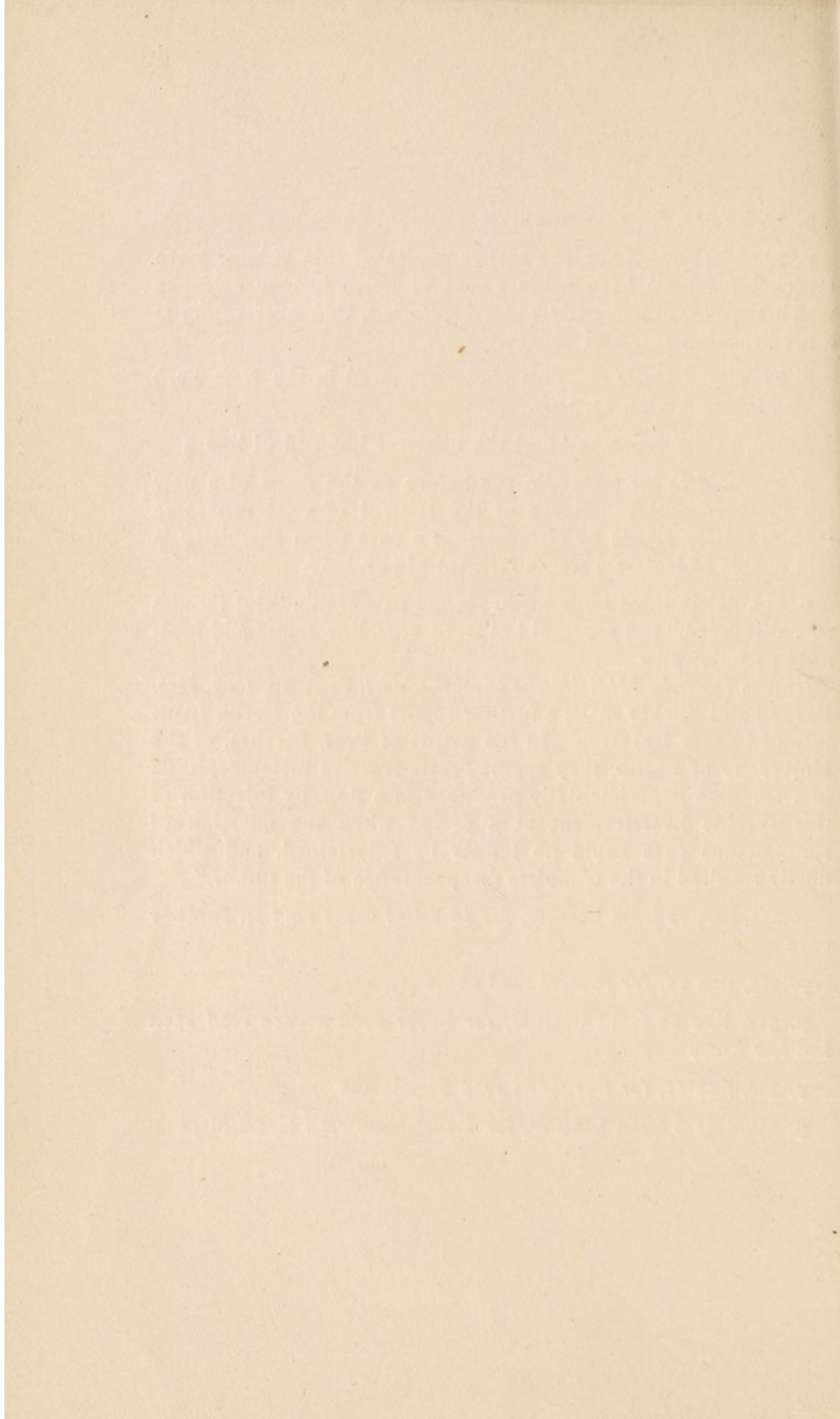
p. 215, line 12 from bottom, *for* In other cases *read* In another case

p. 215, line 15, *for* several *read* some

p. 315, line 13 from bottom, *for* never seen a case *read* seen but few cases

p. 320, line 11, *for* Surgeons *read* Physicians

p. 340, line 6 from bottom, *for* Ezgebnisse *read* Ergebnisse



THE CONQUEST OF CANCER

A PLAN OF CAMPAIGN

BEING AN ACCOUNT OF THE PRINCIPLES AND
PRACTICE HITHERTO OF THE TREATMENT OF
MALIGNANT GROWTHS BY SPECIFIC OR
CANCROTOXIC FERMENTS

BY

C. W. SALEEBY, M. D.

F. R. S. (EDIN.)

*Author of "Worry," "Heredity," "Evolution," "Psychology,"
"Sociology," "Ethics," etc.*

NEW YORK

FREDERICK A. STOKES COMPANY

PUBLISHERS

17960

- 4064981

Copyright, 1907,
BY FREDERICK A. STOKES COMPANY

All Rights Reserved

November, 1907

302028

WELLCOME INSTITUTE LIBRARY	
Coll.	welM0mec
Call	
No.	QZ 200
	1907
	S16c

THIS BOOK IS
DEDICATED
TO
THE CAUSE OF HUMAN LIFE



Digitized by the Internet Archive
in 2019 with funding from
Wellcome Library

<https://archive.org/details/b31356229>

P R E F A C E

BELIEVING, as I do, with Dr. Beard and Prof. Von Leyden and many others after him, that the war with cancer during the past half-century—which comprises practically the whole of the scientific period in medicine—has hitherto been conducted on lines all but unprofitable and irrelevant, as the lamentable failure to obtain practical results only too fully demonstrates, I have called this volume “The Conquest of Cancer” rather than, for instance, “The War with Cancer,” not because I wish to maintain any such monstrously untenable thesis as that the disease has been actually conquered, but because I hold that there is abundant warrant for the belief that the new mode of attack indicated and initiated by Dr. Beard gives us the key to the enemy’s position, and that so soon as this advantage be pressed home, the conquest of cancer will be an accomplished fact. The evidence and the arguments of the succeeding pages are submitted in the belief that they should suffice to direct the attention of the practical worker away from modes of attack which have hitherto proved wholly unprofitable, towards a new mode which commends itself on two distinct counts.

It commends itself because of the favorable results which have already been recorded, in practice, by observers so eminent as Profs. Von Leyden and Bier of the University of Berlin, to name only two of the foremost workers associated with the attack on cancer by means

of specific cancrotoxic ferments, as I propose that they should be called. But though he would be hardy indeed who should question to-day the actual achievement of such results, and though I have necessarily devoted some space to them, the new plan of campaign in the war with cancer commends itself—to those who, however deeply interested, are not themselves the subjects of cancer—far more on rational and abstract grounds. It is based upon the conception of a radical chemical difference between the malignant and the normal cell, upon the conception of fermentation as absolutely the most radical fact of all life, and upon the equally well-attested doctrine of the specific character of ferment action: whilst, on its practical side, the new inquiry regards the rare but indisputable spontaneous cure of the disease as a capital fact and no longer as a mere surgical curiosity. It may be earnestly recommended that when next an indisputable case of spontaneous cure or change in that direction be observed, the patient should no longer be reported on at long and casual intervals as regards the merely local condition, but that, if possible, he be retained for the most exhaustive and prolonged study on the lines of modern clinical pathology. Too much cannot be known regarding the condition of the blood and urine and metabolism generally of such a patient. To the best of my knowledge all such opportunities—which, as I believe, will prove priceless—have hitherto been totally ignored, simply because the war with cancer hitherto has been conducted almost exclusively on surgical lines, without thought of the matters which, directly attention is directed to them, are seen to be fundamental.

Though, in the absence of more authoritative writers, I have constituted myself, amid general censure, the sole

public advocate of the pancreatic ferments since March, 1906, I hold no brief for them; and the fact that they take the most prominent place in the succeeding pages may possibly be nothing more than a historical accident. If, despite what so many observers report them to have accomplished, they prove relatively inefficient as compared with other ferments, known or unknown, tried or untried, I shall certainly never waste another moment in urging their claims. When these came before me, and for some time afterwards, if not—as may be—to-day also, they far surpassed anything proposed or employed as weapons against cancer: if they in their turn can be surpassed I shall as persistently urge the claims of their supersessors as I have hitherto urged their own, and if any one cares to say that I have abandoned trypsin, he is heartily welcome to do so. If and when its superiors be obtainable, by all means let it pass forever from the memory of all but the historian of science.

Whatever the ultimate verdict on trypsin, I shall be well content if the following pages suffice to demonstrate that the pioneer work of Dr. Beard and his followers points the way to all future work upon cancer, immediate and remote; if, in a word, it be demonstrated effectively that the attack upon cancer by means of specific ferments is, because it must necessarily be, not merely the most successful hitherto, but the naturally appointed and indicated means by which this most accursed thing is to be mastered by man.

In the text I attempt to deal with the relations between cancer and surgery, considered from the point of view of actual practice. Here, however, I wish to comment upon their scientific relations. In the pre-scientific days, cancer was naturally a "surgical disease," and, later, the mag-

nificent achievements of Simpson and Lister, which the resistance of contemporary surgeons could not prevent, greatly enlarged the scope of the surgery of cancer. The disease is still considered to be a surgical affection, and its study hitherto has almost entirely been confined to the surgeon and the microscopist. As regards practice, surgery as a whole has a record of the most signal and lamentable failure. The fault may not lie with the surgeons, or not with them wholly, but the fact is indisputable, as common experience and the death-rate from cancer show. But as regards the study of the disease, it has yet to be recognized that the surgeons have failed no less signally. During the sixty years since the introduction of chloroform, millions of cases of cancer have been available for study by the surgeons, and it is doubtful whether they have added anything essential to our knowledge of it except such as is contained in the dictum of Sir James Paget—a surgeon who, like Lister, was so much more than a surgeon—that a cancer is an “imitation-tissue.” The surgeon has his invaluable work to do, but his habit of mind—or, rather, of hand—is not adapted for the study of cancer. In the report of the Middlesex Hospital upon the pancreatic treatment (May, 1907) there is not even included any account of the urine, let alone the blood, of the patients under observation. The fact would be incredible were the report not available to all. The surgeon’s sole interest in cancer, which has been too entirely relegated to him, lies in the question, “Can I cut it out?” He will study with minuteness the channels in which it spreads, since this bears upon operation, and he favors the microscopist, since he hopes—though often deceived—that the microscope will aid him in diagnosis. But, for choice, he prefers the diagnostic

incision. A case of spontaneous cure—who should be retained for study at any fee he cares to ask—is noted as a curiosity, but its overwhelming significance is ignored. The surgeon's knife not being requisitioned, he turns elsewhere; the physician leaves cancer to the surgeons; and the patient whose blood, in all probability, as I believe, holds the secret for which so many ages have sought, is discharged as a "freak."

The surgeon's interest in medical chemistry is practically confined, as any one may observe for himself, to the examination of the urine for albumin or sugar, since these bear upon the suitability of a patient for operation. Lately he has learnt to examine the blood for an excess of white cells, since this often indicates suppuration somewhere. That is almost the limit of his interest in these fields of inquiry.

Now we have to learn that, though cancer has hitherto been treated by the surgeons and left to them to study, it is in no useful sense of the words a "surgical disease." Dislocations and fractures are surgical disorders, and the genius of the surgeon is eminently suited to them. But of all known diseases, without exception, cancer is the furthest from these. It is a phenomenon of cell-life, dependent upon infinitely subtle factors in cell-chemistry. It is a problem in cytology certainly; in cell-chemistry certainly; in embryology certainly, in some cases if not in all, as will be demonstrated in the following pages: and all these things are remote from the surgical province, and commonly looked upon by surgeons as unpractical and visionary. The mechanical aptitudes or habits of hand which make a man a good surgeon, and therefore in his own province an invaluable member of society, tend to be psychologically incompatible with the habits and

interests of mind which are adapted to the study of the essentials of cancer. The notions of a specific form of albumin or a specific ferment do not interest the surgical mind, in the absence of evidence that they can be sewn or excised or put in splints. At this moment Prof. Bier, of Berlin, who was already famous as a thinker as well as an operator, is the solitary living surgeon of any eminence who has concerned himself—publicly, at any rate—with the new mode of inquiry regarding cancer. I desire, then, to direct the attention of the chemist-clinicians, who will spend years of patient labor upon the study of relatively nugatory problems of the urine or the blood, to the problem of cancer, and I dare predict that the first man who will make an exhaustive study of these fluids in a case where cancer is undergoing spontaneous cure will enroll his name permanently in the history of medical science.

From surgery and the surgeons, as they have hitherto worked at the problem, there is nothing more to be hoped. They have pursued one line of inquiry only—the making of their operations extensive enough to effect an extirpation of the disease; these operations have now reached the point at which, in some instances, they kill outright—to render the phrase “primary mortality” in its Anglo-Saxon equivalent—more patients than even survive for the “three-year limit”; and it is evident that no more is to be hoped in this direction. Surgery is literally “manual labor,” and manual labor will not solve the problem of cancer.

The one remaining hope for the surgeons is that the principle of publicity regarding cancer shall be recognized as never heretofore, so that patients may come up for operation at the earliest possible stages of the disease.

A great German surgeon—great on this account alone, apart from any other—has done something in this respect by a systematic newspaper crusade: and, two years ago, I was so convinced of the urgent necessity of some such effort in this country that I asked a prominent English surgeon to write a volume on the subject, which now forms part of the New Library of Medicine. On all hands the surgeons now repudiate the doctrine of non-publicity, which has always found advocates, in theology and medicine and science generally; the doctrine expressed in the proverb about ignorance and bliss and in Pope's line about a "little learning." This doctrine has been a curse and a lie in all ages. A little knowledge is the most that any of us can possess, and it is of priceless value compared with no knowledge at all. A very little knowledge about the first symptoms of cancer at the present day would enable a few of the best surgeons to save many lives; and the failure of the surgeons, until a year or two ago, to use every means in their power to make this little knowledge general is one of the most serious indictments that can be made against their profession in the past.

But I have many more reasons than that already indicated for addressing this volume not only to the medical profession, but also to the public at large. For one, I have placed myself in what, so far as I know, is the unique position of a man who has received a medical education, and is a continuous student of medicine, but who, though not incapacitated by alcohol or private means or old age or illness, does not practice. I have ceased to practice solely because of the liberty which this state permits me in writing or speaking what I believe on medical subjects whenever and wherever I think fit: but

the more liberty the more responsibility, and especially if others are not similarly placed. Hence, I have felt constrained to write whenever and wherever I could concerning what I believed to be of public moment—and of urgent and immediate moment to thousands—regarding cancer. Had it been possible I should have written not merely in the *Contemporary Review* and *Harper's Weekly*, for instance, but also in the *Hibbert Journal* and the *Police News*. And he who would deny the necessity of my continuing in this course must prove his contention. There is some recent history in the following pages which may or may not help him.

A further reason why in this volume I have attempted the all but impossible task of writing for a medical and a non-medical audience at once is that time is a factor in this question. If the new study of cancer and the new methods of treatment based upon it will help patients next year they may help them to-day, and since cancer does not wait for us we must press on with the utmost speed. And if it be necessary that patients or their friends shall make some of the pace for the profession, then so it must be. If every doctor were as keen about the matter as if he had cancer himself, other means would suffice.

A yet further reason for employing wider and more expeditious channels than would otherwise suffice is that the progress of the new study and its application to treatment must largely depend upon the general practitioner, who does by far the greater part of the work of the profession for a beggarly fraction of its material rewards and a still smaller fraction of its honors. He works, if he be competent, from morning till night and from night till morning. It is not his fault that he has very little time for reading; and it does not suffice that he should

rely solely upon the leading medical journals for his guidance in this matter. But he will read what the public compels him to read, and if the public attention is directed to this book, I believe that he, and therefore the cancer-patient, will find in it the record of work done which, since it is not of my doing, I am free to describe as of priceless value in my opinion; and also many indications of work remaining to be done in which he can share.

Yet another and urgent reason for publicity, as I show in the sequel, is the extreme likelihood that, failing a preventive prophecy, a "cancer-serum," in effect proprietary, though not openly patented, and having as its basis some ferment or ferments, may any day be put forward and exploited, not in the interests of the public, but to swell the pocket of some mercenary, such as neither examinations nor the Hippocratic Oath, nor any conceivable means except the education of the public, can keep out of the noble profession of medicine.

The addition of an index would have delayed publication for a fortnight. I apologise for its absence. One is being prepared and will be added as soon as possible. The price of the book has been kept as low as possible, and on this account I have omitted to include illustrations of the microscopic appearances of aberrant germ-cells, trophoblast and cancer. I desire to acknowledge the help received from many editors on both sides of the Atlantic, from my publishers for their energy and sympathy, and from my friend and literary agent, Mr. Curtis Brown, who has been my right hand in the matter of obtaining publicity for more than a year past. I note also that, when opportunity offers, I hope to arrange in a special chapter the discussion, hitherto neglected, of the blood in cancer.

I *know*, as a matter of repeated personal observation, that the articles which have brought me so much abuse from the Powers that Be in this country have directly led to such boons for not a few stricken patients as perfect ease instead of uncontrollable agony, and sweetness for intolerable fœtor: and unless Nature has ceased to be consistent and chaos is come again, I am assured that similar and greater results may follow this book at any time; and that, if it directs the attention of workers at cancer to the lines on which alone the conquest of the disease is to be attained, the present gains in life and happiness will be as nothing to those that will follow: and it is in this belief that, against the urgent advice of my friends and the instinct of self-protection, I send it forth. The first case of cancer I ever saw destroyed my religious orthodoxy before I left the operating theatre, and seared my soul for life; it is an abominable affront to the dignity of man, a disease that makes a goblin of the sun and almost brands the optimist of any school as a deliberate and imbecile liar. If this book, despite all its faults of ignorance or style or taste or judgment, or any others—faults due in part at least to haste, for I have believed myself to be racing for life against time—serves even in infinitesimal measure to hasten the end of this most damnable thing, my life will have been worth living, though it should end upon the gallows amid universal execration.

C. W. S.

13 GREVILLE PLACE, N. W.,
October, 1907.

CONTENTS

PART I.—THEORETICAL

CHAPTER I.—INTRODUCTION

	PAGE
No truth sterile—Money not the first necessity of science— Individuality and progress.....	3

CHAPTER II.—THE ALTERNATION OF GENERATIONS

Instances from primitive forms—Alternation amongst ver- tebrates, fish and chick—The nature of trophoblast— The observation of Prof. Farmer.....	13
--	----

CHAPTER III.—GERM-CELLS

The continuity of germ-cells—Work of Nussbaum, Weis- mann and Beard—Aberrant germ-cells, their origin, situation and possibilities—The germ-cell theory and Cohnheim's theory.....	23
---	----

CHAPTER IV.—CANCER-CELLS AND TROPHOBLAST

The cellular pathology—Cellular function and structure— Characters of the cancer-cell, indefinite multiplication and specific digestion—Trophoblastic cells—Their cancerous behavior—Anatomical resemblance between cancer-cells and trophoblast-cells—Chorio-epithelioma or trophoblas-	
--	--

	PAGE
toma—The condition of its origin—Physiological resemblance between cancer-cells and trophoblast-cells—Production of higher tissues in malignant growth—The relation between identical twins and malignant growth—Teratomas and dermoid tumors—Recent implicit acceptance of the trophoblast theory of cancer...	31
 CHAPTER V.—THE PANCREAS 	
Its position, function and structure—Its ferments—Their origin and activation—Their innocuousness—The history of the pancreas in the individual—Its activity before birth.....	50
 CHAPTER VI.—THE EVOLUTION OF THE DISCOVERY 	
The trophoblast theory, 1902—Suggestion regarding ferments, 1904.....	59
 CHAPTER VII.—THE IMMEDIATE CAUSES OF CANCER 	
The predisposing causes—Irritation as such insufficient—Possibility of reversion on the part of the somatic cell—Cancer and heredity—Cancer and failure of the pancreas—The absorption of trypsin from the bowel—The case of the "Fletcherite"—Cancer and intestinal decomposition	64
 CHAPTER VIII.—THE MICROSCOPIC STUDY OF CANCER 	
Failure of this method—Excessive attention to cell shape—The differences mere masquerade—Supersession of the microscopic method—Astronomical analogy from the telescope and the spectroscope—The microscopic method now superseded by the chemical method.....	74

CONTENTS

xxi

CHAPTER IX.—LIFE AND FERMENTATION

	PAGE
Life a series of fermentations—The theories of Liebig and Pasteur—The nature of ferments—Their mode of action—The specific nature of ferment action from Pasteur to Fischer.....	83

CHAPTER X.—THE CHEMISTRY OF CANCER

Pasteur the pioneer—His work with tartaric acid—The asymmetry of the carbon atom—Dr. Beard's speculation correlating this with the alternation of generations	93
---	----

PART II.—PRACTICAL

CHAPTER XI.—CANCER AND SURGERY

Recent advance in the surgery of cancer—Its extraneous difficulties—Its substantial failure even to-day—The consequences of imperfect operation, including those made for diagnostic purposes—The work of Paget and Von Leyden—The ferments to be employed in addition to surgery when practiced—Condemnation of imperfect operations, <i>i.e.</i> nearly all operations—Fallacious beliefs regarding the results of operation—Hope from surgery existent in only a minute percentage of cases—The results of modern radical operations—Dr. Beard's opinion as to the place of surgery.....	109
---	-----

CHAPTER XII.—THE PREPARATION OF THE FERMENTS

Grave and numerous difficulties—Most preparations now on the market worthless—The standardization of the ferments—Results of tests—The make-up of the ferments—The question of dilution—The question of keeping—Ferments in hot countries—Outlines of a sound	
---	--

	PAGE
method—Recommendations to the chemists and to practitioners—This whole subject still <i>in embryo</i>	137

CHAPTER XIII.—THE DETAILS OF TREATMENT

Choice of preparations—The oral administration—Probably more valuable than formerly supposed—Von Leyden's work on this subject—Local application and its results—Hypodermic application beset with difficulties—Must not be made into the tumor—The process of sterilization—Duration of treatment—The question of dosage—This whole subject also still <i>in embryo</i> —A wide field for inquiry—The recent paper of Dr. Copeman—The use of alkalies as adjuvants—The excretion of the ferments—Possible prevention of cancer.....	160
--	-----

CHAPTER XIV.—THE GENERAL ACTION OF THE FERMENTS

The action of the ferments in health—Increase of weight—Trypsin not a poison—Excretion of trypsin—The local reaction, entirely accidental and to be avoided as highly detrimental—The general reaction in cases of cancer—The work of Dr. Cleaves—The "trypto-glycogenic" reaction—Action upon the kidneys.....	185
---	-----

CHAPTER XV.—THE GERMAN WORK

The earlier work of Profs. Blumenthal and Bergell—The specific action of trypsin upon cancer in the test-tube—The work of Prof. Von Leyden—Abandonment of the microscopic method—The specific albumins of cancer and their specific destruction by trypsin—Demonstration of the absorption of trypsin when given by the mouth—Theoretical questions involved—Von Leyden's results by mouth administration and by injection into the tumor—The specific action of trypsin on cancer	
--	--

CONTENTS

xxiii

	PAGE
demonstrated—The work of Schütze and Bergell, disproving the formation of anti-trypsin—Von Leyden's later work with a liver ferment—His theory as to the origin of cancer—The work of Prof. Bier with the ferments of the blood—Definite results obtained—The question as to the origin of these ferments—The possible use of normal human blood in cancer—The preliminary report of Pinkuss and Pinkus—Prolonged study of injections—Anti-bodies formed when sterile solutions of decomposed pancreas were employed—No anti-trypsin formation after use of Fairchild preparations—Results obtained in four cases—The authors pursuing their inquiry—The work of Blumenthal—The specific nature and chemistry of the cancer-cell—The specific action of trypsin upon it—These conclusions confirmed by others.....	195

CHAPTER XVI.—SOME RESULTS RECORDED HITHERTO

Dr. Beard's results in the mouse—Confirmation by Zanoni—The work of Odier—The reports of Rice, Morton, Wiggin, Campbell, Luther, Cleaves, Doran and others in America—Recent results in Great Britain, the reports of Cutfield, Meggitt, Cavanagh and Matthews—General comments.....	234
--	-----

CHAPTER XVII.—THE CLAIMS OF THE TREATMENT

The action of the ferments upon dead cancer tissue—Absolute freedom from danger when properly employed—The relief of fœtor—The relief of pain—The ferment treatment claimed to supersede morphia—The relief of cachexia—Conditions that prevent success: previous operation, the possibility of immunizing the tumor, the possibility of reversal of ferment action—Applicability to all cases—Further discussion of difficulties—The influence of the treatment upon the leucocytes—Possible

	PAGE
fallacies: mistaken diagnosis, spontaneous cure—Some replies to critics.....	251
CHAPTER XVIII.—SOME WARNINGS	
The risk of a secret serum based upon trypsin and amylopsin or other ferments—Secrecy and dishonesty may be regarded as equivalent—Warning against the unqualified cancer-quack—Warning against the so-called cancer specialist.....	285
CHAPTER XIX.—AMYLOPSIN AND ECLAMPSIA	
Dr. Beard's theory as to the nature of eclampsia—Resemblance between its symptoms and those which may follow the death of cancer under treatment by trypsin—Speculation as to the possibility that amylopsin may be remedial in eclampsia.....	296
—	
PART III.—SOCIOLOGICAL	
CHAPTER XX.—THE POWERS THAT BE	
The conditions of progress—Principle of authority in science—History of anæsthesia, antiseptis, inoculation for small-pox, vaccination and hypnotism—The recent behavior of the powers that be— <i>The Medical Press and Circular</i> — <i>The Practitioner</i> — <i>The Hospital</i> — <i>The Lancet</i> — <i>The British Medical Journal</i> —The contrasted behavior of the <i>Journal of the General Practitioner</i> —The Imperial Cancer Research Fund—The Middlesex Hospital and its report.....	303
CHAPTER XXI.—CONCLUSION	
Personal explanation—The risks of officialism—Huxley's warning—The author's warning against himself—The value of faith in science—The value of love in science..	351

PART I—THEORETICAL

THE CONQUEST OF CANCER

CHAPTER I

INTRODUCTION

I HERE propose to discuss at length what I believe will, in its full fruition, prove to be one of the most remarkable and valuable discoveries ever made by the genius of man. It is of immediate value, because it already involves, in some degree at any rate, the relief of the most horrible and common of incurable diseases, against which, hitherto, the knife alone has been of any avail—and that desperate remedy itself almost invariably outwitted at last. But even this discovery would not be of such universal interest were it not for the many facts of great significance which have attended it—facts which, quite apart from the humanitarian question, bear upon the general principles of progress both as regards science and as regards society.

The work of Dr. Beard, in the first place, furnishes an illustration that has never been surpassed of the mighty truth that there can be no sterile truth; and it is to this great proposition that I must devote the first few pages of my book. I have no intention of neglecting the practical aspects of the matter, and the reader will have no difficulty in turning, when he pleases, to my discussion

of them; but in a volume destined for the public, as well as the medical profession, they cannot take the first place; that belongs by right to the discussion of matters which concern all who think, whether or not they be practitioners of medicine or men threatened with malignant disease.

To one who asked him what was the use of a modest and new-born truth, the promise of which for human life was apparent only to the eye of philosophic faith, Benjamin Franklin replied, "What is the use of a baby?" His question is one of the best answers on record. Yet, admirable though it be, it is scarcely adequate to express the fact. There are babies and babies, and some of them, whether from inherent or external causes, may become much worse than useless; but of no truth is this true, for all truths are of one and the same order, and that order is perfection itself. Every smallest and meanest fact is part of the universal whole. In the world of knowledge there is no analogue whatever to the baby that is degenerate or diseased, and there can no more be an ultimately useless truth than an ultimately useful lie. "No belief which is contrary to truth can be really useful," said John Stuart Mill, and no belief which is consonant with truth can be really useless.

These things, of course, are commonplaces. They are amongst those many commonplaces which only rare persons actively believe. In her war with nescience, science needs money which, though the least important part of the sinews of war—as we shall see—is yet not very readily dispensed with; and men are entitled to ask, when money is requested of them, whether or not it will accomplish anything of real value to the life of man. The poor we have always with us, and their appeals cannot be unheard.

Is it a warrantable thing that on this needy earth men and money should be spent upon the gathering of that which is not bread? Must not we distinguish once and for all—or at least until many of our crying evils have been silenced forever—between useful and useless knowledge? With so little done and so much to do, is it well that, for instance, a man who might be of real immediate use to the community should devote years of his life to a minute description of the various stages in the development of the skate or the chick?

Only one answer, I believe, could be returned to this question, if it were possible, as it is not, to admit the assumption that knowledge can be divided into the useful and the useless. I will even admit to a feeling of annoyance at seeing men of science attack problems, the solution of which would seem to be of no immediate moment, whilst more vital matters remain neglected. But a case like that which we are about to discuss should teach one the unwisdom of these distinctions. Not only is there no sterile truth, but it is frequently found that facts which seem to be of the least moment may be the most fruitful. Of the development of the skate, Dr. Beard said to himself, "Here are a series of changes which have never yet been completely delineated. I will follow them from the beginning to the end." Not even he could have conceivably predicted that he would thereby be led to the theory of alternation of generations in vertebrates, to the trophoblastic theory of cancer, to its control by ferments, and, I believe, to the initiation of a new era of therapeutics.

"You are wasting your time!" they said to Pasteur, a promising young chemist, when he turned aside to study the behavior of bacteria. To Dumas and Biot,

great chemists though they were, it was not given to pierce the veil of the future, and see those pioneer researches blossom into the tree, the leaves of which are for the healing of the nations. I place these two instances side by side for their significance. As some imbecile critic has remarked, Dr. Beard is "not even a medical man"; nor was Pasteur a medical man. The chemist, in his study of fermentation, found it necessary to inquire into the behavior of microbes. The embryologist, in his study of development, found it necessary to follow up the life-histories of certain kinds of cells. Each was following truth for her own sake; secure in the faith that, if a fact be true, the question of its utility is already answered. Neither can have had at first even the glimmerings of any notion that his work was destined within his own lifetime and for all ages to succeed, to close the doors of men's homes in the very face of advancing death. But such are the rewards with which truth will crown those who follow her wherever she leads, without fear or favor, and for nothing but the love of her *beaux yeux*.

When, therefore, we are inclined to murmur and declare that this man or that, working at what appeals to him, has no claims upon us, let us remember such instances as these. You cannot dictate to a man in what he shall find his chief interest. It may be inexplicable to us that a man should prefer to work at this when we ourselves would prefer him to work at that, but so it is. These preferences will determine not merely the work in which the worker is happiest, but the work which he does best; and it is the quality of his work and not its subject matter that will in the last resort determine its utility. Mankind will therefore chiefly profit when he does the work which it pleases him to do. This may be

of an apparently insignificant, or even trivial, kind; it may seem to be as remote from human life as the remotest star. It may be destitute of that romance which, in the case of astronomy, is always added to its unquestionable utility. The work may deal with very small things, such as bacteria, which one can scarcely see, and which the foolish will therefore suppose to be not worth seeing. The worker may be utterly unable to throw out any large hints of what his work will achieve; he may, or may not, imagine himself to be a mere bricklayer in the house of truth, but it does not matter that he cannot answer our questionings.

The only matters into which we can rightly inquire are these: Are the bricks well and truly laid? is the workman honest with himself? has he an eye to the main chance, or is his work its own reward? does he record what he observes, and not what he wishes to observe? does he quote the evidence against his view as well as the evidence for it?—in a word, does he answer to the definition of Tyndall, "There is in the true man of science a desire stronger than the wish to have his beliefs upheld, viz., the desire to have them true"? If these questions can be answered as they should be, we must be satisfied, no matter whether the workman be concerned with beetles, or skates, or double stars, or electrons, or savage customs, or with the immediate treatment of some crying evil of the day.

It is, perhaps, not chiefly money, however, that the man of science requires, but rather elbow-room and respect. In these days there can be no question that science requires for its most rapid advance the endowment of research, but that is not the great thing. Hundreds of

thousands of pounds have been given for cancer research. In England a single donation of no less than £40,000 was made long after Dr. Beard had done his work. All the money thus given entirely failed to achieve the desired end. Worse than that, much of it served for a considerable period, and still serves, to delay the recognition of Dr. Beard's work and the realization of its value. The worker who, single-handed, made the first great step, did so almost entirely at his own expense, and in the hours which he could spare from his official duties. Almost all the external help he received was a few shillings to defray the expense of experiments on mice—which he undertook not in order to verify his work, but in order to draw attention to it.

There are many other problems, and not only medical problems, which still await solution in the interests of mankind. Some of them, the needs of which are recognized, may have the services of official workers, with funds at their disposal and high patronage behind them. Such workers are to be judged not by their position, but by the quality of their work. Far be it from me to say a word against the accordance of public support to such enterprises, but meanwhile let the educated public look with a discerning eye upon workers who, without encouragement, or salves, or stipend, are attacking the same problems. Their methods and modes of approach may be totally distinct from those favored by the official workers, and their opinions may be very discordant, but the chances are always in favor of the amateur in the true sense of that word, as against the hireling. This last may also have the love of truth, but the amateur has nothing else, and his strength is as the strength of ten because his heart is pure. He is liable to be looked upon as a

crank. Simpson and Pasteur and Lister were all called cranks in their day, and Dr. Beard was called a "cancer crank" in a responsible medical monthly long after his work was launched, and the saving of lives had been authoritatively reported.

Of course a man seems to be a crank who has ideas peculiar to himself on any subject. But when thousands of students have been working at a problem for decades and their united labors have amounted to nothing substantial at all, the man who has peculiar ideas is just the man who is wanted. Dr. Beard has solved the problem of cancer, as I propose in this book to show, because he built upon knowledge peculiar to himself—knowledge of his own discovering. All the recognized doors were closed. Dr. Beard made a door of his own, and forced an entrance by it. Until the facts were too many for his opponents of course he was called a crank: naturally his papers were refused by the editors of the leading medical journals; naturally the same fate awaited the letters in which he traversed demonstrably erroneous, if not deliberately false, statements.

The second great lesson, then, which we may learn from this case is the old lesson which men have been taught from the beginning of history, but which only the very few in any generation have learnt, that individuality is the sole instrument of all progress, that "nothing was ever yet done which some one was not the first to do," and that, therefore, the new must always get a hearing. As Mill says, "Genius can only breathe freely in an atmosphere of freedom," and Milton, pleading the same cause, speaks of "Liberty, which is the nurse of all great wits."

Therefore, whenever, or wherever, in matters of

science or in any other matter, there is heard, half stifled, a solitary voice saying that which academies and corporations and churches and governments do not say, I for one must prick up my ears. The man is *ipso facto* a crank, like Socrates, and a greater than Socrates; and may be nothing more. But those who have read the history of thought with opened eyes will ever give a free hearing to him who can be heard only with difficulty, for it is from such as he that everything yet achieved by man has proceeded.

Religious toleration is essentially a modern achievement, in so far as it has been achieved; and there are those who say that, after all, it depends for its existence upon a fundamental skepticism. But the history of science is no less important and instructive in its demonstration of the supreme value of freedom of thought and speech. And the sad fact is that human nature, quite apart from religious influences, finds tolerance so difficult even in matters of science. The cry always is "Can any good come out of Nazareth?" For years and years Lord Rosse's great discovery of the spiral nebulæ was discredited by all academic astronomers; was he not an amateur, and was it not likely that he had mistaken for a nebula a spiral scratch on the object glass of his telescope? I have chosen an instance from a remote science, and one in which the new discovery could affect no one's purse. How much more serious is the case when a great corporation finds itself instructed by an outsider, and when this instruction involves serious monetary loss—not necessarily to all the members of the corporation, but to those who will not be instructed?

Our lesson, then, is that we must prove all things, and not least the things which are asserted by those who have

no authority whatever. If they are wrong they will come to naught; but they may be right; and beware, "Lest haply ye be found even to fight against God."

In preparation for this book I have lately re-read two famous treatises, which would not seem, perhaps, to bear immediately upon the subject of cancer—the *Areopagitica* of Milton, and John Stuart Mill's essay *On Liberty*. The case which we are about to discuss might be used to illustrate almost every one of the arguments—they are the same arguments in both cases—employed by these two great writers. The two points which I have already tried to make, are: Firstly, the value of all truth; and secondly, the importance of the individual and his liberty. The reader will find these discussed in noble language and with irresistible force by the writers I have named. He can scarcely realize, perhaps, how strange was my experience in reading those two works again, after eighteen months of hard fighting for Dr. Beard. But, after all, they are accessible to any of us, and the only substantial value of a contemporary illustration of their propositions is to be found in the fact that it *is* contemporary—the fact that men have not yet learnt their lessons. Yet I cannot refrain from comment on at least two fine sentences from Milton. He says of truth, "Let her and falsehood grapple; who ever knew truth put to the worse, in a free and open encounter? . . . For who knows not that truth is strong, next to the Almighty; she needs no policies nor stratagems nor licensings to make her victorious; those are the shifts and the defenses that error uses against her power."

Now certainly the present is a case in point. Truth has had no policies nor stratagems nor licensings; all that has been asked for from the first was a fair hearing and

a fair trial. On the other hand, these shifts have certainly been used against her, and in forms as contemptible as they can possibly assume—forms including not merely ordinary misrepresentation but the downright assertion of what was not true. Yet truth is now winning; and her triumph is acknowledged in the United States and Germany, if not at home. Nor need we be displeased, on the whole, with the result; even though the delay in victory may still be costing many valuable lives. After all, the power of a free press has vindicated itself, and it would not be easy to name any great discovery in therapeutics that won assent in a shorter time than will suffice for this.

So much, then, by way of introduction. Let us now trace from the beginning the main steps of the work which will ere long attain a splendid culmination.

CHAPTER II

THE ALTERNATION OF GENERATIONS

IN the early years of the nineteenth century there was discovered the fact that sometimes a living organism "produces an offspring very unlike itself, which by and by gives origin to a form like the parent." These facts were generalized in 1842 under the now familiar term, "the alternation of generations," by Steenstrup, who described the "natural phenomena of an animal producing an offspring, which at no time resembles its parent but which itself brings forth a progeny that returns in its form and nature to the parent."¹

The alternation of generations usually involves what Geddes and Thomson define as a "rhythm between sexual and asexual reproduction." I quote what they describe as the clearest case of the kind:—

"A sessile, plant-like zoophyte, which buds off numerous nutritive persons, produces in the warm months modified individuals which are set adrift as medusoid persons. Unlike the hydroid which bore them, these become sexual, and from their fertilized ova an embryo develops, which eventually settles down to start a new sessile colony. And thus through the seasons we have hydroids asexually producing sexual medusoids, and these again producing hydroids. The life-history for two complete

¹I am indebted for this quotation to the admirable account of this subject contained in Geddes and Thomson's *Evolution of Sex*.

rhythms may be written in the formula, in which M, F, and A stand for male, female, and asexual forms respectively:

$$\frac{M}{F} - A - \frac{M}{F} - A - \frac{M}{F}."$$

Many other instances might be quoted, but they all may be included under the above formula. In some of them, perhaps the greater number, it is the sexual generation that is the most prominent, but the embryo produced by this generation is asexual, and from it the sexual generation is again produced. In the case of the animal kingdom it is commonly asserted that alternation of generations cannot be found above the very humble creatures known as tunicates. In plants, however, this alternation, which is extremely conspicuous in many cases, has been recognized more or less easily throughout the whole series of all but the lowest forms. This is to say that even the flowering plants, including of course the trees, which occupy the same place in the vegetable kingdom that the vertebrates hold in the animal kingdom, still display an alternation of generations. In them, however, it is the asexual generation or sporophyte that is so extremely conspicuous, whilst the sexual generation is a mere appendage to it.

It is now more than fifteen years since Dr. Beard asserted that even amongst vertebrate animals, as amongst the flowering plants, there is an alternation of generations. This conclusion was first stated in a short paper which is now of historical interest.² References to it

²"A Supposed Law of Metazoan Development," *Anat. Anz.* Vol. 8. Jena, Gustav Fischer. 1892.

may be found in the text-books, but they are very brief, and it is only now, I suppose, that this paper will receive the attention which it deserves. The solution of the problem of cancer was really involved in that paper, though, as I have already hinted, no one could have made such a prediction, nor was Dr. Beard concerned at that time to do anything but demonstrate the facts which he had discovered.

These facts were really based upon his study of the early development of a fish, which he began in September, 1888. I have before me, as I write, twenty-three papers of various lengths which have been published by Dr. Beard during the last seventeen years, the first being communicated by Professor Huxley to the Royal Society, and received April 20, 1889. In that paper Dr. Beard first described the presence within the Bill-fish (*Lepidosteus osseus*) and other fishes, of certain curious cells, which seemed to play a temporary part in development and then totally disappeared. This led to the paper above named, from which I may quote a few words. After describing the presence of the larval or asexual form in many of the lower Metazoa,³ and pointing out "the analogy which would obtain between the suggested mode of Metazoan development and the accepted fact of an alternation of generations in the life-histories of all plants above the lowest Thallophytes," Dr. Beard says:

"I venture to attach most weight to the application of the principle to the vertebrata. . . . It is undoubtedly the obstacles offered by the phenomena of vertebrate development which have hitherto prevented the enunciation of the law of development as an alternation of generations. Larvæ are so commonly encountered among the

³Metazoa are all animals above the simplest or protozoa.

invertebrata that the wonder is that no one has inquired why they are so rare in any guise in the vertebrata." Dr. Beard goes on to assert that larval structures can be found in several Amphibia and Fishes, and that these degenerate. Speaking of one such structure, he says: "It is gradually broken down by some ferment action."⁴ Dr. Beard's conclusion is that "Metazoan development appears to me to be by means of an alternation of generations in that, from the fertilized organism arises the larva, upon which, in one way or another, according to the circumstances of each case, a new form, the adult, or *imago*, takes its origin." Fifteen years have elapsed. It has been found that, just as, in various of the invertebrates, the egg gives rise to a larva which does not directly develop into the new organism, but "serves as the foundation on which the development recommences, as it were *de novo*"; so, according to Dr. Beard, in such vertebrates as the skate and chick, there is found to be an asexual larval stage, upon which the embryo proper develops. Such are the embryological beginnings which have led, as we shall see, to the discovery of a specific and naturally appointed remedy for cancer.

It is Dr. Beard's belief that the alternation of generations is common to all vertebrates, including man. What then becomes of the asexual stage or generation, since there is no sign of it in the adult individual? In the early development of the skate and the chick, Dr. Beard has discovered what he calls a "critical period," which marks the beginning of the disappearance of the transitory larval generation that has hitherto been growing. We may call the characteristic tissue of which this struc-

*We shall hereafter note the splendid triumph of this small truth within fifteen years.

ture is composed by the convenient name of *trophoblast*. Dr. Beard appears to have shown that up to the critical period in the case, for instance, of the fish, all the digestive processes have depended upon an acid, intracellular digestion, very similar to that which occurs in the stomach of the adult. The critical period is determined by the development in the embryo of a new organ called the pancreas (or sweet-bread). In each of us this is the most important organ of digestion. It produces various ferments, the most important of which is known as trypsin. This substance acts only in an alkaline, or neutral, or *very faintly* acid, medium, being thus contrasted with pepsin. Writing in the *Lancet* nearly three years ago, Dr. Beard said:⁵

“At this epoch, the critical period, the fish commences to feed itself on yolk, not by an [intracellular] acid, peptic digestion, but by an alkaline, pancreatic one. The commencing activities of the pancreas during foetal life initiate an alkaline digestion by the means of the most powerful and important of all the digestive juices, the pancreatic. . . . If the secretion be absent, neither the asexual structures of a fish development nor the cells of chorio-epithelioma [a tumor made of normal trophoblast] do, or can, degenerate. The solution of the problem of the functional relation of embryo and trophoblast—how the latter nourishes itself by an [intracellular] acid digestion, and degenerates slowly by a pancreatic digestion—becomes at the same time the embryological, if not the medical, resolution of the problems of malignant neoplasms. . . .”⁶

⁵February 4, 1905.

⁶In a thesis presented to University College, London, by Dr. J. M. Hamill, in 1907, the identity of trypsinogen, the antecedent of trypsin, in all vertebrates is demonstrated.

In the above quotation there is involved the whole trophoblastic theory of cancer, and the treatment based upon it. The argument is that a cancer consists of trophoblast, and that the digestive substance or substances which cause the degeneration of normal trophoblast will also cause the degeneration of abnormal trophoblast. It has been my object in the present chapter, however, merely to discuss Dr. Beard's theory of the alternation of generations in the vertebrates, including man, together with his assertion that the tissue called trophoblast represents the asexual generation, and the further and all-important assertion that the *normal* arrest of growth of this tissue, its death and digestion, are due to the activities of the pancreas, which, in the case of man, begins to function actively at the seventh week of development—the "critical period."

But let us be perfectly clear in our minds as to the origin of this trophoblast, on the theory that it is really the asexual generation in man. This must be clearly stated before we can go on in the next chapter to discuss the manner in which abnormal or irresponsible trophoblast—in other words, malignant tissue—is asserted by Dr. Beard to take its origin.

According to the theory of alternation of generations, the larval, asexual or trophoblastic stage in the history of man arises, of course, from a fertilized germ-cell. The common view hitherto has been that the union of the sexual elements produces a new single cell from which the new individual arises, there being no intermediate stage. On this new theory, however, we assert that an asexual generation is interpolated—in other words, the fertilized germ-cell does not directly give rise to a new individual, but to this asexual stage or larva

composed of the tissue called trophoblast. The new individual which is to become a human being is the child of this larva, and actually arises in, and upon, it. The larva is thus in a sense its wet nurse—to use the term of Steenstrup.

It follows, therefore, that it is part of the essential and necessary nature of the germ-cell, if it develop at all, to develop not directly into a new human being, but into the tissue called trophoblast. That assertion is involved in the theory of alternation of generations. If, then, there be in any part of a man's body—as, for instance, his lip—such a germ-cell, and if that germ-cell be aroused to growth and division from any cause, it will develop into trophoblastic tissue, which will have the essential characters of normal trophoblastic tissue, and which, if it is to be destroyed at all, will be destroyed as normal trophoblastic tissue is destroyed.

But plainly, it is necessary to inquire into the apparently wild assumption that a germ-cell, capable of such developments—or incapable of them—should occur in a man's lip. "*Que diable allait-il faire dans cette galère?*" That is the question which we must attempt to answer in the light of Dr. Beard's work upon germ-cells, which is discussed in the following chapter.

Meanwhile, however, it is desirable, I think, to look a little more closely into this question, difficult though it be, of the alternation of generations, as Dr. Beard recognizes it in the case of the higher animals. Amongst other reasons for doing so is the fact that Dr. Beard's theory beautifully accounts for, and includes an interesting observation on, the intimate structure of cancer-cells as observed by Messrs. Farmer, Walker and Moore in the year 1903. These observers were able to recog-

nize, in many of the cells of certain malignant growths, a characteristic type of division such as had previously been recognized to be characteristic of the formation of germ-cells.⁷ The special fact of this division is to be found in the nuclei of the cells. The stainable or chromatic matter in the nucleus of a cell is broken up, before division, into a number of small bodies—the number of which is fixed for any species of animal or plant—called chromosomes, and the peculiarity of the division which is to form a germ-cell is that the characteristic number of chromosomes is halved. At some future date, when the germ-cell unites with one from an individual of the opposite sex, the proper number of chromosomes is restored. It is by no means in every case that this characteristic and remarkable type of cell division can be observed in malignant growths. We may readily understand that it is not every tumor which will go so far in reproducing the cycle of development. The fact, however, is not only explicable on Dr. Beard's theory, but might indeed have been predicted from it. He commented on this fact in the *Lancet*, October 29, 1904, and I will quote one or two sentences. "For it is an inalienable property of the trophoblast of normal development that upon it germ-cells arise. Once these have come into existence, it is but a question of a certain limited number of cell divisions before they present the phenomena associated by many embryologists with the reduction of chromosomes. In short, the proof furnished by the researches of Farmer, Moore and Walker, and confirmed by Bashford and Murray, of the occurrence

⁷"Resemblance is exhibited by the cells of malignant growths in man and those of normal reproductive tissue." (The *Lancet*, December 26, 1903, p. 1830.)

of divisions in cancer- and sarcoma-cells usually associated with the maturation of germ-cells, was the one thing lacking to establish beyond question the true nature of a malignant tumor as the pre-embryonic portion of the life-cycle, the asexual generation. While at present it would be wrong to assume that such cell divisions must of necessity occur at some time or other in all malignant tumors, for even a malignant tumor may conceivably be so reduced or retrograded as to be unable to repeat the whole cycle of the germ-cells, just as no tumor is known to form actual sperms, it is now beyond doubt that the occurrence of such divisions in certain cases proves a malignant neoplasm to be the pre-embryonic portion of the life-cycle. It is a life-cycle with the embryo omitted. Germ-cells never do arise and never could have arisen from somatic or embryonic cells or tissues."

If we trace upwards the evolution of the vegetable kingdom, we find an important alteration in the relative magnitude of the sexual and asexual generations. Low down in the vegetable kingdom the great bulk of the species is constituted by asexual generation, and very little by the other. But vegetable evolution has been accompanied by a gradual increase of the asexual generation, together with a reduction in the importance of the sexual generation. Hence, in the higher plants almost everything that we notice is the asexual generation. This is to say that the fertilized egg, in the cells of which the full number of chromosomes has been restored, gives rise to the flowering plant with which we are so familiar. On the other hand, the sexual generation is merely represented by the spore stage of the plant, in which the number of chromosomes is reduced, and which has no free existence, but remains enclosed in the tissues of the flow-

ering plant or asexual generation until fertilization occurs. This, of course, doubles the number of chromosomes, and initiates the asexual generation again.

Now what is the case of the animal? In it the fertilized egg gives rise, as Dr. Beard has taught us, to the trophoblast, which is therefore the analogue of the flowering plant, though it is as insignificant as the flowering plant is conspicuous. This trophoblast has the characteristic of yielding germ-cells, and on occasion these may actually show ripening and reduction of the chromosomes, as observed by Prof. Farmer and his associates in the case of cancer. Normal trophoblast, however, yields many primary germ-cells, one of which becomes the embryo, whilst the rest, as we are about to see, are included within that embryo—most of them in one special spot, but some in abnormal situations. Occasionally two primary germ-cells may develop completely and independently, and the result is the production of what are called identical twins, two individuals, invariably of the same sex, and extraordinarily similar in physical characters.

I am aware that this subject is extremely difficult, yet I have only briefly alluded to it. For further details and for a valuable table of the comparison between the life-cycles of the animal and the plant, the scientific reader may be referred to Dr. Beard's paper on "The Interlude of Cancer," *New York Medical Record*, February 2, 1907.

CHAPTER III

GERM-CELLS

SEVERAL years have now elapsed since Prof. August Weismann, the great biologist of Freiburg, enunciated his famous theory of the "continuity of the germ-plasm." Therein he repudiated a belief in the continuity of germ-cells, and it is in that simpler form that we must first study the idea—which we owe to Nussbaum. It is an error to imagine that the germ-cells found normally situated in the body of any of the higher animals or plants are products of that body. On the contrary, they have an independent origin. According to Nussbaum's view, if we trace the normal development of a fertilized ovum, we find that it gives rise to two distinct sets of cells; the one set are those which will develop into the body of the individual with all its various tissues; the other set remain germ-cells throughout, so that they are continuous with the preceding germ-cells, and though they are in the body, are not of it. I may quote the words in which I have previously expressed this theory. "Ideally stated, the sequence—actually observed in many animals—is as follows: The germ-cells and the body-cells grow up side by side. The germ-cells are shed and give rise again to a new body and to their own undifferentiated descendants, which that new body temporarily shelters. The germ-cells are immortal; the individual is merely a temporary host which shelters a few generations of the

germ-cells, whose unbroken continuity constitutes the race. Plainly, the likeness of daughter and mother begins to be intelligible. The germ-cells of the mother—which will develop into her daughter—are directly continuous with the cells which gave rise to the body of the mother. ‘As the sex-cells in an offspring are thus genetically continuous with [*i.e.* directly derived from] the parental sex-cells which gave rise to it, they will in turn develop into organisms like the parent—a conception fundamental to an understanding of inheritance and development.’ On this theory we must regard each individual as merely the temporary host of the continuous line of germ-cells which constitute the race.”

Now though in many of the lower animals the actual unbroken sequence of the germ-cells from one generation to another could positively be detected, in higher animals, and notably in most plants, it was not thought possible to recognize the germ-cells until a late period in the development of the individual. “In such cases, then, it is impossible to demonstrate any continuity between the germ-cells of an individual and the germ-cells of its parent. But Weismann has shown that it is not, therefore, necessary to abandon the invaluable concept of continuity. He very reasonably assumes that the essential part of each germ-cell is not, for instance, the cell-membrane, or the cellular shape, but a particular kind of living matter—the germ-plasm. He supposes, then, that in the development of each individual a portion of the germ-plasm contained in the parental ovum is not used up in the formation of the offspring, but is reserved unchanged for the formation of the germinal cells of the following generation. Though there is not always a continuity of germ-cells from generation to generation—as there de-

monstrably is in many animals—there is always, in all the animals and plants which display this mode of reproduction, a ‘*continuity of the germ-plasm.*’ From the point of view of the race, the individual is merely the ephemeral bearer of the immortal germ-plasm, which is as old as the race and is subject to no law of death.”

Weismann employed the phrase “germ-plasm” since he was unable to demonstrate the actual continuity of germ-cells in every case. Dr. Beard, however, believes that he has demonstrated the actual continuity of germ-cells *as cells* from generation to generation even in higher animals. If we take a special instance, such as the smooth skate (*Raja batis*), which Dr. Beard began to study nearly twenty years ago, we find, according to him, that an actual continuity of germ-cells is demonstrable. When he examined the very young skate—and the same is true of many other fishes and of the chick—he found that the germ-cells are by no means confined to their proper and characteristic site in the body. He has found them in the head, the skin, the gill-region, the liver, the blood, “in fine, there is hardly a place in the whole trunk or head in which such aberrant germ-cells have not been observed.” He has figured them again and again. There is no possibility of mistaking their identity under the microscope. Where have these aberrant germ-cells come from—these cells, the malign possibilities of which are soon to be indicated? The common view would be that they had wandered from the part of the body of the embryo which gives rise to the germ-cells. But to Weismann or Dr. Beard such an assertion is nonsensical; the germ-cells are older than the embryo. They are not products of any part of the body of the individual; they have arisen outside the embryo and have migrated into it. Dr. Beard

has proved that this is so. In the smallest embryos of the skate no germ-cells are visible. Later on germ-cells appear, but only a very few of them are found in their characteristic site in the body. For instance, in embryos 20 millimeters long, 50 per cent. of the germ-cells are misplaced, whilst in embryos half as long again only about 30 per cent. are misplaced. In the very youngest embryos, containing no germ-cells, hosts of germ-cells are to be found lying in the (trophoblastic) tissue immediately outside the embryo and preparing to enter it. In a word, the germ-cells precede the embryo, and gradually wander into it as it develops. Many of the germ-cells never reach the proper position. They wander along what is called the germinal path, but may find themselves misplaced in all parts of the body. Commonly their fate is to degenerate, but apparently they do not always do so.

It follows that the germ-cells, not being developed from the embryo, are products of the original cell (the fertilized ovum) which always gives rise to the embryo itself. Thus the germ-cells within the embryo are its own immature "twin" brothers and sisters—in other words, the embryo is the product of one of the primary germ-cells, while the remainder come to be regarded, quite erroneously, as its own sexual products.

Let us consider now the case of these aberrant germ-cells which Dr. Beard finds in so many parts of the body. If they do not degenerate, they may yet presumably lie quiescent throughout the whole life of the individual that nourishes them. On the other hand, they may be roused to development; and so we may ask ourselves: "What are the circumstances which, in a given part of a given individual, cause the growth and multiplication of cells which have always been present in him, but which have

hitherto been quiescent?" This question was asked, of course, long before the trophoblastic theory of cancer was advanced, but it is not a question with which Dr. Beard has concerned himself at all. Chronic irritation seems to be undoubtedly one such circumstance, but there are probably many others. The new theory of cancer does not concern itself with this question; at present it in no way tells us anything not formerly known as to the prevention of cancer. Hence if we are to use the word cause in the ridiculous fashion of common speech, which assumes that, for any given fact, there is only one cause—as if the universal past were not the cause of any one fact—we may say that the cause of cancer remains unknown. Why certain cells, latent from the first, should multiply and become patent at this place but not at that, in your neighbor but not in you—we cannot say. *But so far as the control of cancer is concerned, our ignorance does not matter.* I do not wish to say anything so foolish as that the question of the causes which arouse these germ-cells to develop is without interest. The immediate local causes giving rise to cancer have long been studied, and of course it is well that they should be known and avoided. General causes, also, have been suspected—not general causes in the sense that the blood is infected and that the disease has no particular locality, but general causes which may arouse the possibilities in a given locality. By an extraordinary chance there has lately been advanced the theory that cancer is due to a defect in the activity of the pancreas, the trypsin of which, in defiance of all the facts, was supposed to be able to digest glycogen or animal starch. This is the so-called glycogen theory of cancer, part of which has unfortunately been transferred to the germ-cell theory.

Dr. Beard, however, has never declared that an aberrant germ-cell is roused to activity in consequence of the withdrawal of the controlling influence of the pancreas. There is no evidence to show that the action of the pancreas is defective at the start in cancer patients, though this might possibly be so.

Assume, however, that from some cause or other, more frequently operative, as it appears, with advancing years, there may develop and multiply an aberrant germ-cell which is such that if its history had taken a normal course it would have developed into a brother or sister of the individual in whom it occurs. Such a cell, if it develop at a very early stage in the history of the individual—as may sometimes happen, apparently—may form one of those extraordinary tumors which show distinct signs of the attempt to produce a second individual. Such tumors are, as a rule, *not* malignant, but they have long been a standing puzzle to pathologists. It is not possible here to describe the extraordinary cases that are on record. They include many unthinkable monstrosities.¹

Far more commonly, however, this aberrant germ-cell, say in the lip of an elderly man, reproduces the sexual stage or generation consisting of the trophoblastic tissue which we have already discussed. The trophoblast theory, then, asserts, in a word, that a cancer results from the attempt of an aberrant germ-cell to continue its life-cycle, the attempt having ended merely in the indefinite production of larval, asexual or trophoblastic tissue.

If all malignant tumors are products of such aberrant germ-cells, a death from cancer is, so to speak, a case of

¹See the next chapter.

fratricide, since the individual and the tumor which kills him are derived from twin germ-cells.

If this theory be correct, the conditions which lead to the destruction, digestion, and complete absorption of the normal trophoblastic tissue that begins to vanish at the "critical period," should have similar effects upon "irresponsible trophoblast." In a word, *trypsin should cure cancer* by killing and digesting its cells. The rest of the pancreatic secretion should destroy and dispose of the products of this digestion.

This germ-cell or germinal theory of cancer must be absolutely distinguished from an older theory to which it bears a superficial resemblance. The view has always been popular and reasonable that the original cell or cells of a cancer were, from the beginning, different from the cells surrounding them. The famous pathologist, Cohnheim, for instance, conceived the theory of what are called "embryonic rests"—the word being better translated as "residues." He supposed that during the development of the body or embryo, "some of the embryonic cells which should have gone to form definite structures, get shut off, and remain shut off, from the rest of the organism. They retain powers of proliferation and growth, and if at any time they exhibit these powers, cancer results." For instance, certain cells belonging to the external or epiblastic layer of the embryo might become misplaced, lying perhaps in tissues formed from a different layer, such as the middle layer, or mesoblast. Such embryonic residues, Cohnheim supposed, might lie dormant for years, giving rise to trouble only when some special cause excited them to growth.

This theory agrees with Dr. Beard's only in asserting a special character from the first for the original cell of

a cancer—a belief which the recent work of Prof. Blumenthal in Berlin strongly confirms. The embryonic theory asserts that this cell is a cell from one of the layers of the embryo. The germ-cell theory asserts that it is of much older origin than that. It is just precisely *not any cell of any part* of the embryo. It never has been, and never will be, a proper part of that individual at all. It is the possible beginner of a different individual. That is the fundamental point: though the parent cancer-cell has been in the body ever since a very early stage, it is in no proper sense a part of the body.

Furthermore, the tissue to which this germ-cell gives rise is no more epiblastic or mesoblastic than the germ-cell itself. It is larval or trophoblast tissue, belonging to the opposed stage in the cycle of development. It may imitate in certain cases various kinds of tissues, familiar to us elsewhere, and Sir James Paget was profoundly right when he declared that cancer is an imitation tissue. It is that and no more. It is to be hoped that, after this explanation, no one will propose to identify the embryonic theory of cancer with the germ-cell theory; this last traces a cancer to a cell which, so far from being any part of the embryo, is older than any part of the embryo, and has actually travelled into the body of the embryo from without; it states the origin of cancer to be in a germ-cell, and its nature to be that of trophoblast.

CHAPTER IV

CANCER AND TROPHOBLAST

HAVING considered the chief characters of germ-cells, and stated Dr. Beard's theory of their occurrence in abnormal places, and the possibility of their development into malignant tumors, let us now consider the characters of the cells of which these tumors consist. This is evidently the logical place for such a discussion in the new theory of malignant disease, but in point of fact our knowledge of cancer-cells, in nearly everything but the one essential, is much older than this theory.

We should have long ago abandoned forever—in its older form, at any rate—the theory that cancer or any other disease is due to disorder of the blood. It suffices to observe that the blood is itself a product of the cells of the body, and that its state does not determine their health or disease (except where poisons are introduced into it from without), but is rather the index of their health or disease. We know now that the essential living part of every living thing is composed of units called cells; and as all physiology—that is to say, the whole study of the functions of the normal body—must now and hereafter be expressed in terms of the cell, so all pathology—or study of disease—must be similarly expressed. We owe the recognition of this truth, which is expressed as the “cellular pathology,” to Rudolf Virchow. Now if the conception of the cellular path-

ology is true anywhere it is pre-eminently true in the case of cancer—a disease which consists in the multiplication of certain living cells at the expense of their surroundings, and ultimately at the cost of their host's death, and their own.

These cancer-cells vary very widely in many characters, but all agree in essentials. Examined under the microscope, those of one tumor may show scarcely any resemblance at all to those of another. It may be said that almost every known kind of cell, so far as appearances are concerned, may be found in a cancer or other malignant tumor. For many years past, pathologists and surgeons have devoted a vast amount of labor to the study of the various appearances of malignant cells. These appearances have led to the coining of a whole host of names, and painstaking observers have sustained long controversies as to whether this or that kind of tumor is, or is not, really the same as some other kind, or whether it is worthy of being ranked as a sub-class or variety, or what not. These sterile discussions of classification have been modified sometimes by the consideration of the behavior of the cells, such as their degree of malignancy, but always the chief subject of argument and assertion has been the appearances of the cells as they are seen under the microscope. Hence, for instance, such phrases (which might be multiplied indefinitely) as round-celled sarcoma, spindle-celled sarcoma, squamous-celled carcinoma, adenoma, epithelioma, and so on. The cells of some of these tumors resemble nothing found in the normal body, the cells of others show a striking resemblance to those of the tissues in which they arise—this, indeed, being so marked in many cases that the resemblance led to the belief in a real iden-

tity between the normal and the morbid cells, modified only by the exhibition of unlimited growth on the part of the latter.

From the point of view of the student of general biology, there has always been apparent a lack of insight and of an eye for essentials in these discussions. The biologist knows, having been taught by Lamarck and by Spencer after him, that function precedes and creates structure. This is the historical fact of evolution, and the historical fact of the individual also. It always has to be reckoned with, though it is so constantly forgotten by the physiologist and the pathologist who, coming in at the end of the process and seeing certain structures associated with certain functions, can scarcely help fancying that structure comes first, and that the function is a consequence of it. This is an abstruse and fascinating question which I cannot pursue here, but I would insist upon what seems to me to be its pertinence to the matter in hand. In the light of Lamarck's conception we shall be more likely to regard as unessential the various appearances presented by cancer-cells, reminding ourselves that their structure, as in the case of all living things, is merely a means adopted, and adapted, for the purpose of displaying their vital functions; and we shall proceed to ask ourselves what those vital functions are.

Then it is that, despite, for instance, their resemblance under the microscope, we begin to realize how profoundly the cells that *look* like gland-cells in a particular cancer, differ from the cells that *are* gland-cells among which it is growing. It used to be said that the malignant cells differed merely in having broken loose from the general bodily control. The process was a local rebellion. These phrases are trivial and nonsensical—once questioned,

they are doomed. Brushing aside all the resemblances in structure—resemblances which are not at all to be found in many cases, be it remembered—we begin to realize that the essentials of vital behavior in the case of the body-cell and the cancer-cell are radically opposed. What then, are the characters of the cancer-cell, it being granted that we are to think of essentials and not of the mere outline architecture of the cell?

These characters have long been known in a general way, though it was left to the individual genius of Dr. Beard to explain them. If it be adequately nourished from without, the cancer-cell is capable of indefinite multiplication. It is of an extremely low order of development, and is almost incapable of differentiating itself. The blood-vessels within the midst of a cancer have invariably grown into it from without; no cancer-cell, so long as it remains a cancer-cell, is capable of giving rise to anything but another cell like itself. This general absence of any power of differentiation is an extremely marked and significant characteristic. The cancer-cell is also distinguished by its high vitality: but though it produces substances which enable it to destroy every living tissue with which it comes in contact, and even the lifeless structure which forms part of bony tissue—yet it is itself readily susceptible to the action of certain deleterious agencies. Cancer-cells die in large numbers, for instance, as the result of the attacks of microbes, thus giving rise to many of the most distressing symptoms of the disease, and producing dangerous substances which are absorbed, causing the chronic poisoning of the patient. It has been attempted, without success, to destroy cancers by the injection of bacterial poisons.

But we have not yet emphasized what is the most marked and the most deadly characteristic of the cancer-cell. The phrase indefinite multiplication does not at all suggest this characteristic. Cells may multiply indefinitely, and cause huge tumors, constituting, perhaps, a nuisance by their weight or their pressure—and yet these, not having the essential character of cancer-cells, are merely innocent or “benign” tumors. Similarly also, cells multiply in every case of local or general inflammation. Paying too much attention to this multiplication, many pathologists and surgeons have endeavored to demonstrate a real identity between the phenomena of inflammation and of benign and malignant tumors. But there remains a real *differentia*—which, it is true, makes the indefinite multiplication possible, but which is not found in association with other cell multiplications. *The cardinal fact of the cancer-cell is that in the course of its life, quite apart from its multiplication, it digests and destroys the living cells of the individual in whom it is growing.* This it seems to do in virtue of the possession of a ferment which was discovered by Eugen Petry in 1899, and which Dr. Beard has called *malignin*. This acts in an acid medium, and it seems to be certain that the fluids proper to a cancer are possessed of an acid reaction. Now we have arrived at something real and significant, as distinguished from any mere question of the shapes of cells. We have ascertained a fundamental fact as to the function, as to the essential vital behavior, of the cancer-cell. After all, the failure of the previous observers was only due to the natural tendency which we all display in forming our first judgments of men as well as cells. But just as the real nature of a man, the real man, is not constituted by his shape, but by what he

is and does, so also the real nature of a malignant cell is forever hidden from the microscope. We know the cancer-cell not by its outline, but by its acts.

Dr. Beard, then, was well content to leave to others the discussion of the shapes of cancer-cells, whilst he, having recognized the triviality of that question, could proceed to think about them in terms of their essentials. A cancer-cell, large or small, round or spindle-shaped, is always a cell which thrives by eating into the tissues around it, and in the course of its growth, thus achieved, divides and multiplies.

TROPHOBLASTIC CELLS

None of the facts just stated were discovered by Dr. Beard. Except for the recognition of the cancer ferment, they have all been known for many years. His advantage in their contemplation merely lay in the fact that he looked at the essentials. In point of fact, it has long been evident to all who thought for themselves that the cancer problem was a problem of cell chemistry. Here were certain cells which, whatever they looked like, were fundamentally different from the ordinary cells of the body. The difference was one of function, to be expressed in chemical terms, and of course it follows that there must necessarily be, if we could find it, or make it, at least one substance which would interfere with the chain of chemical reactions in the case of the one kind of cells, whilst it would not interfere in the case of the others. This proposition is a necessary inference from the assumption of a fundamental difference in chemistry, which was in its turn an inference from the observed

facts of difference in vital behavior. Dr. Beard has found the substance in question—or one such substance—as will be proved up to the hilt in the sequel; and he has found it because of no lucky chance, but because of his previous researches in embryology. His study of the vital characters of the cancer-cells suggested to him as irresistible the belief that these cells are fundamentally identical with the cells composing the tissue called trophoblast, and, therefore, he argued, *that which normally arrests the growth of a trophoblast must therapeutically arrest the growth of a cancer.*

The cells composing trophoblastic tissue are highly uniform in their behavior and also in their appearance. Let us consider first of all their behavior, which, as we have insisted, is all-essential. Like the cells of a cancer, the cells of a trophoblast multiply indefinitely. That is important so far, but it is by no means conclusive in any way, since, as we have seen, indefinite multiplication of cells is found in circumstances utterly different from those we are considering. Trophoblastic cells, again, like cancer-cells, are of an extremely low order of development, and do not show any general differentiation into tissues. Most important of all, the cells of a trophoblast thrive and multiply by eating into the surrounding structures—these in normal development being maternal structures. *This attack upon maternal structures is absolutely indistinguishable from the attack of a cancer upon its surroundings, and possesses all the same essential features.* The identity is admitted by all recent students.

Yet, again, the mere appearance of trophoblast has a most significant resemblance to the appearance of certain malignant tumors. Dr. Beard has long asserted what, indeed, is evident to any one who will look for himself,

that it is absolutely impossible, even under the highest powers of the microscope, or by the use of any variety of staining dyes, to distinguish between specimens of trophoblast and specimens admittedly taken from certain typical and malignant tumors. Such tumors present appearances utterly unlike those of any normal tissue except trophoblast, whilst from it they cannot be distinguished. Fail to mark the slides you prepare, and if once you mix them you can never sort them out again.

Hence, again, the proposition that the substance of a malignant tumor is trophoblastic.

If normal trophoblast, then, begins to degenerate and disappear at the very time when the pancreas of the developing individual first shows signs of activity—as proved by microscopic examination of its cells—may it not be that it is the activity of the pancreatic secretion which effects the digestion of normal trophoblast? Dr. Beard had long known that, to take the case of man, the critical period, as he calls it, occurs at the seventh week, and he had also known, as a fact of another subject, so to speak, that the pancreas shows its first signs of activity at the seventh week. But it was not until the coincidence in time was presented to his mind, with the immediate suggestion of more than coincidence between the two facts, that he saw the light. For if the pancreatic secretion digests and destroys normal trophoblast, it must also be capable of destroying abnormal or irresponsible trophoblast, already believed by him to be the proper definition of a cancer.

At this point, however, the critical reader will very properly observe that it is not for me, who have insisted upon the relative insignificance of the mere appearance

of cancer-cells under the microscope, to lay much, if any, stress upon the structural resemblance between trophoblastic cells and those of certain malignant tumors: and I admit the validity of the objection. But we have already observed that normal trophoblastic tissue eats into the maternal structures which surround it, and now we have to observe the proved and accepted fact that normal trophoblast may give rise to a malignant tumor. Not very many years have passed since pathologists first identified the appalling kind of tumor which is now called chorio-epithelioma. Under certain conditions this may arise during pregnancy. Its origin is in the womb, which it attacks, and from which it spreads, by the lymph-vessels and the veins, to various parts of the body, often giving rise, for instance, to secondary growths in the lungs, or brain, or both. Formerly chorio-epithelioma was supposed to be divisible into a malign and a benign variety, but now it is believed that the disease is always essentially malignant. Further, chorio-epithelioma is now recognized as the most malignant of all tumors.

Its name is derived from the chorion, one of the structures peculiar to the developing foetus. This chorion helps to form the placenta, or "after-birth"—a cake-like organ which furnishes the connection between the developing foetus and the mother. The placenta is usually described as consisting of a maternal and a foetal portion. The latter is, in part, developed from the membrane called the chorion. The external portion of the chorion consists of a layer of cells—the "trophoblast" of Hubrecht—which have the business, in virtue of their peculiar and significant power, of eating into the tissue of the womb at the spot where, as the result of this process, the placenta will be formed. Sometimes, how-

ever, this process is not limited, as it should be, but the trophoblastic cells continue their destructive work, and then constitute, as I have said, a chorio-epithelioma so called—much better named trophoblastoma. It is a known fact, then, that, *whether or not cancers in general are made of trophoblastic tissue, there is one form of cancer which is certainly so made.* It possesses in pre-eminent degree the characteristic and essential properties of cancerous tissue—the power of unlimited growth, and the power of digesting, or breaking down by ferment action, the tissues in its neighborhood. It also possesses in high degree the power of forming secondary growths.

I have said that, normally, the development of the trophoblast is limited, and, recognizing its power of unlimited multiplication, we must ask what it is that limits it. The answer given by Dr. Beard, as we have seen, is that it is the activity of the pancreas—which is known to be active before birth, though it has no food to digest—that results in the formation of trypsin and the degeneration of the trophoblast.

Now if this answer be the true one, we must expect to find certain facts of the pancreas associated with those known cases in which the trophoblast does not cease to develop as it should, but continues to grow and multiply, first in the wall of the womb, and later in the mother's body generally. What, then, are the cases in which chorio-epithelioma—or trophoblastoma, as it should really be called—does develop? *They are cases in which the fœtal pancreas does not perform its function.* This tumor arises in cases where the embryo dies before the critical period, or where the fœtus or embryo—the name given to the child in its earliest stages—is expelled prematurely, *leaving its chorion behind it,* or in cases where the

fœtus undergoes mal-development, so that its pancreas is not formed and active. Of all the theoretical arguments for Dr. Beard's view, there is none more cogent than this—that *a kind of tumor, admittedly cancerous in all essentials, arises from normal trophoblastic tissue in certain cases of pregnancy, where the pancreas of the child, for one reason or another, is not in action.* This is the fact, and in the light of our other knowledge it admits of only one interpretation.¹

There are a number of further facts for which an interpretation is now provided by the theory that cancer-cells and cells of the peculiar reproductive tissue called trophoblast are essentially identical. I will here note some of these.

It is admitted that the Röntgen rays in certain cases have a specific toxic action upon cancer-cells, just as trypsin has. Now the Röntgen rays have also been shown quite lately to have a specific toxic action upon the characteristic cells of the reproductive organs, so as actually to cause sterility, whether in the male or the female. We realize now the complete erroneousness of the old assumption that the cells of the reproductive organs—such as the ovary, which is significantly one of the commonest sites of tumors—are to be regarded as passive except on special and exceptional occasions. We know now that continuous processes of great complexity and importance occur in these organs during the reproductive ages. In our present state of ignorance regarding their nature I can do no more than merely note the fact—which, like all other facts, must have an

¹I believe it will be generally recognized, before long, that the so-called "myxoma of the chorion" is only a less malignant form of chorio-epithelioma, and that its development from the trophoblast depends upon similar conditions.

interpretation—that one and the same agent, the Röntgen ray, has a specific action both upon malignant cells and upon some stage or other in the life-history of germ-cells.

Here also I will state again, on account of its importance, the remarkable resemblance in behavior between the process of erosion, as it is seen in a cancer, and the process of erosion by which the trophoblastic tissue, or chorionic epithelium, in normal pregnancy, eats its way into the tissues of the uterus.

Further, we must note the extremely high vitality of the cancer-cell. The almost universal teaching hitherto—and most amazing teaching it is—has been that the cancer-cell is of very low vitality. This opinion would seem to depend upon the fashion in which exposed tumors are attacked by the germs of suppuration and putrefaction. But if we consider for a moment what the history of cancer is, we recognize at once that an extraordinarily high vitality is a chief character of the cancer-cell. Now it shares this character with the cells of trophoblast, the powers of which we have already noted, and especially their character of unlimited reproduction.

An immensely significant fact, the importance of which it is impossible to overestimate, is that certain kinds of malignant tumors are capable of developing in them higher elements, such as even cartilage, bone and primitive muscle. I regard this fact as absolutely conclusive in its indications. No tissue in the higher animals but germinal tissue could conceivably do such a thing; no other tissue could conceivably have in it the potentialities —“determinants,” to use the phraseology of Weismann —of these highly differentiated structures. It is notably the kind of malignant tumor usually described as the

large spindle-celled sarcoma that sometimes evolves these higher tissues within it.

I have mentioned elsewhere, but repeat here, the demonstration that the cells of a cancer frequently divide in a peculiar and highly characteristic fashion, formerly thought to be peculiar to the processes of cell division that lead up to the formation of mature germ-cells. Now, according to Dr. Beard's theory, cancer as trophoblastic tissue should be expected occasionally to demonstrate the power of giving rise to germ-cells.

The commonest site of tumors is the germ-cell tissue—that is to say, the specific cells of the ovary.

For myself I do not care to exclude the possibility that in some cases cancer may arise in cells which were formerly proper tissue-cells of the part in question, but which from some cause or another have undergone a reversion to the germ-cell state. The student of cell-life will not find such a conception incredible. In this connection I would note that malignant tumors have never been found to occur in three tissues—namely, in fatty or adipose tissue, in striped muscular tissue and in nervous tissue. (Tumors of the brain arise never from the nervous elements, but from the connective tissue elements—which bear the same relation to the nerve-cells as a house does to its inhabitants.) Now these three kinds of tissue are probably the most highly differentiated in the body; differing as widely as possible in all other respects, they agree in this. The nerve-cell is so much differentiated and specialized that it is quite incapable of multiplication—in accordance with Spencer's famous law of the antagonism between individuation and genesis. The same is probably true of the striped muscle-cell, there being reason to believe that when a muscle is devel-

oped by exercise, the previously functioning cell-fibres do not divide, the growth being due to the development of small round cells which had not previously developed. Hence there is a limit to the growth of every muscle as to the growth of every brain. As for the fat-cell, it has almost specialized itself to extinction, very nearly the whole of its bulk consisting of lifeless oil. It seems to me that we may perhaps understand why it is that malignant tumors never arise in these three tissues, if we assume the process of specialization to have gone so far that reversion to the primitive state, common to all of them, is impossible. This suggestion is merely thrown out for what it may be worth, and I am quite aware that, if there is anything in it, it involves the modification of some non-essential parts of Dr. Beard's theory.

One other remarkable fact, first discussed by Dr. Beard, bears very closely on this question of the relation between reproductive and malignant tissue. It is that every stage can be traced, or at any rate that every intermediate condition has been observed, between, on the one hand, unquestionably malignant growths, and, at the other extreme, the production of what are called identical twins—twins invariably of the same sex, and not infrequently all but indistinguishable from one another. Now Dr. Beard has been asserting for years that a malignant tumor arises from a germ-cell, such that if it had undergone normal development at the proper time, it would have been the twin brother or sister of the individual in whom the tumor arises. I will confess that when first I met that statement of Dr. Beard's, it seemed to me too wild and bizarre for credence; yet now, as I have said, we have the recognized and accepted fact that the students of these matters have observed all stages between

say, a malignant tumor of the ovary at the one extreme, and identical twins at the other.

The countless varieties of monstrosity, such as the inclusion of one more or less imperfect and "parasitic" twin within another, pass by gradual stages in one direction to the occurrence of a typical malignant tumor in a complete and living individual, and in the other to the production of a pair of healthy twins. In the light of this fact I would remind the reader of the statement already made, that, according to Dr. Beard's theory, the death inflicted by cancer is really a fratricide.

In this connection I must mention the very strange group of tumors which are described as dermoid tumors, owing to the fact that they always contain skin or mucous membrane, occurring where neither skin nor mucous membrane has any business to be. Many dermoids are apt to be confused with so-called teratomas, or tumors consisting of a monstrosity. "A teratoma," says Mr. Bland Sutton, in his article, "Tumors," in the *Encyclopædia Medica*, "is an irregular, conglomerate mass containing the tissues and segments of viscera of a suppressed foetus attached to an otherwise normal individual." Now certain dermoids seem undoubtedly to be due to the inclusion of portions of skin below the skin-surface and their development there. The importance of these is small, for we know that sometimes the accidental puncture of the skin, pushing a portion of it below the surface, may give rise to a small tumor. This is merely the growth of misplaced skin, and has nothing to do with our subject. Moles also are really dermoids, but as they sometimes give rise to malignant tumors, and as the tissue underlying a mole has a structure resembling that of certain malignant tumors, they are of

more importance; but here I wish especially to refer to the most common variety of dermoid tumors, which are called "ovarian dermoids." These are cystic, or more or less hollow, tumors, which occur very frequently in the ovary—that is, in the proper germ-cell tissue—and contain such things as mucous membrane, skin, hair, teeth, horn and bone. Fine growths of hair and remarkably perfect teeth are not infrequently found in them. It is difficult to believe that there can be any fundamental distinction between a teratoma—a sort of jumble of the organs and tissues that should have made an individual—and an ovarian dermoid that contains not merely skin and structures derived from, or cognate with, skin, such as teeth and hair, but also bone, which has a totally different origin. I believe that the key to the whole of this hitherto uncharted area of pathology has now been placed in our hands. It is especially the recent knowledge of this subject that bears upon the general question before us. In Mr. Bland Sutton's admirable article, for instance, which was published in 1902, there is no reference at all to the possibility that a teratoma—this jumble of a second individual—may ever be malignant. But now the existence of malignant teratomas is well recognized, and evidently it is of the utmost importance in still further filling up the interval, which has now been completely filled up, between the malignant ovarian tumor at the one extreme, and the production of identical twins at the other.

Lastly, I would observe that the commonest of all tumors are the cystic tumors of the ovary, and that all stages have been observed between them and malignant tumors of this organ. I believe that we shall yet treat

“cystic ovary” by means of trypsin and amylopsin, or other ferments.

Though Dr. Beard and all his works were rigorously ignored at the meetings of the British Medical Association both in 1906 and 1907, at the latter meeting Professor Swayne, of Bristol, read a paper on Chorio-epithelioma, which is of interest to us here. (*British Medical Journal*, Aug. 24, 1907, p. 440.) The author remarks that, in studying the ovum of the hedgehog, Hubrecht “showed the development of the ‘trophoblast’² by proliferation and thickening of the outer layer of the primitive epiblast, with, around the trophoblast, coincident destruction of maternal tissues, which latter was of a temporary nature only, equilibrium between the edacious properties of the trophoblast and the resistance of the maternal tissues being eventually obtained; the Peters³ ovum exhibited similar processes.”

Here it may be noted that Dr. Beard’s explanation of the arrest of the growth of the trophoblast is totally ignored and an explanation offered which is exactly similar to that of Molière’s physician, who “explained” the hypnotic power of opium as due to its *vis dormitiva*.

The author notes the work of another observer, who showed that the trophoblast, even in normal conception, “manifests up to a certain point of the development of the ovum characteristics simulating those of malignant growth, which are lost when the resistance of the ma-

²“What is this ‘trophoblast’? Has any one besides Dr. Beard seen it?” I have been asked. Doctors are not learned in embryology, and they are little to blame therefor; but the fact should deter them from hasty criticism of embryological reasoning.

³A human ovum.

ternal tissues is able to overpower the edacious (*i.e.* digestive) properties of the trophoblast."

The subsequent paragraphs of this paper show how nearly it is possible to approach the trophoblastic theory of malignant tumors without mentioning or recognizing it. The author quotes several recorded cases in which growths "apparently identical" with chorio-epithelioma—*i.e.* trophoblast the growth of which is abnormally permitted to continue—have occurred not only in cases where conception had not occurred at all, *but also in males!* For instance, Andrews found trophoblastic tissue in a sarcoma of the femur, or thigh-bone. Schlangenhauer in 1902 reported two cases in males, one of a sarcoma of the testicle, with secondary growths, "the tumors having the structure of chorio-epithelioma," while in the other the structure reproduced not only the trophoblast itself, but even certain of the tissues which lie immediately underneath it.

In the ensuing discussion, Prof. Strassman, of Berlin, commented upon the occurrence of these tumors in males, and suggested that "a new view of the etiology (causation) of these tumors will be discovered." But no one alluded to the view advanced by Dr. Beard nearly three years before.

The critical student may perhaps consider that when epithelioma of the chorion is found to occur *in the male*, the slavery in which we are held by language has reached intolerable limits. I refer to this paper because it instances the fashion in which Dr. Beard's work is ignored by physicians, and because of its relevance to the discussion, in another chapter, of the manner in which the microscopic study of cancer has become a fetish: so that when a structure resembling that of trophoblast is

found in a male, it is labelled chorio-epithelioma, while the obvious processes of thought are arrested by the spectacle. If chorio-epithelioma—that is to say, a tumor consisting of trophoblast—is admitted to occur in the male, and to constitute certain tumors of bone, it will seem to most people that the trophoblastic theory of malignant growths requires no further admission. For the very inaccurate phrase, chorio-epithelioma, let us substitute a correct one, trophoblastoma, not because names are things but because incorrect naming prejudices thinking. Trophoblastic tissue, then, has been found to constitute malignant growths in the male; this fact is familiar to all students of malignant diseases: and can be stated in a discussion amongst experts without allusion to the theory of Dr. Beard.

I submit the self-evident proposition that the admitted occurrence of tissue obviously trophoblastic in so-called sarcoma of bone, and in the male, is the absolute confirmation of Dr. Beard's theory so far as these malignant tumors were concerned; and most forcibly suggests the likelihood that other malignant tumors are really of similar nature. As to cases of chorio-epithelioma, or, rather, trophoblastoma, arising in the testicle, *i.e.* in the germ-cell tissue of the male, it is obvious that here is further evidence of Dr. Beard's views.

CHAPTER V

THE PANCREAS

THE pancreas is a gland several inches long, which lies in the upper and back part of the abdomen, being stretched right across the body. It is usually described as having a head which is placed at the right and a tail which reaches far round to the left. The general appearance of the gland is not inaccurately suggested by the sweetbread which constitutes a table delicacy. It appears, however, that all sweetbreads provided by the butcher are not pancreas, but that this popular name is applied indifferently both to the pancreas and to another edible gland which is found in the upper part of the chest, and is called the thymus. There passes from the pancreas a duct or tube which can, indeed, be traced throughout the whole length of the gland, gradually becoming larger as it passes from the tail to the head. This duct conveys the secretion of the pancreas to the bowel only a very few inches below the stomach, so that when the contents of that organ are passed on they are promptly subjected to the action of the pancreatic juice.

Essentially, of course, the pancreas is a collection of living cells, and these are of a highly characteristic kind. They are evidently secreting cells, and if they are examined in the absurdly so-called "resting stage"—that is to say, the stage during which they are doing their work—they are found to be manufacturing within them a great

mass of tiny grains which can be very distinctly seen. If now the acid contents of the stomach enter the bowel, these grains disappear, while at the same time a fluid secretion is poured through the duct of the gland into the bowel where it is required. Let us then consider the composition of this secretion, and let us do so in the light of the most recent knowledge. The older mode of statement, and one to which there is no serious objection for some purposes, is that the pancreas produces a secretion which contains, apart from unimportant substances, certain ferments—amongst them being one which digests proteids or albumins and is called trypsin, another which digests starchy matters and is called amylopsin, and a third which digests fat and is called steapsin. But let us first consider the case of the trypsin, which has been very exhaustively studied.

It is perfectly evident that if trypsin is to be found in the pancreas gland, and if trypsin prevents the growth of cancer, cancer of the pancreas should be unknown. On the contrary, this is a very well recognized site of cancer. This argument has been urged, of course, against Dr. Beard's theory, and since it really looks like a valid argument, it has occupied a practically unique place in the controversy—if controversy it can be called. Unlike mere abuse or misstatement, this requires an answer.

Now the fact of the matter is, as has been known for some years, that the living pancreas never contains any trypsin. I may quote, for instance, from the article on "Nutrition" in the current edition of the *Encyclopædia Britannica* (vol. xvii, p. 674), and thereafter we shall see that even the clear statements which were there made as long ago as 1884 fall short of the whole truth. The writer says:

“The pancreas, when perfectly fresh and just removed from the yet warm body of an animal which is killed, does not contain, ready formed, all ferments which will in the sequel be referred to as characterizing the pancreatic juice. If we treat the gland, for instance, with glycerin, which possesses the power of extracting and dissolving all the ferments, we fail to obtain a solution which possesses the power of digesting proteids; but, instead, we find a substance in the solution from which, by the addition of a little acetic acid, the proteolytic ferment may be formed. The cells of the pancreas thus elaborate a substance which is the antecedent of the proteolytic ferment, and which yields it when it passes into the pancreatic ducts: it is customary to speak of this body as *zymogen*, or ferment-former, because it gives rise to one of the chief enzymes or ferments of the juice.”

This was written nearly a quarter of a century ago, and is in itself a quite sufficient answer to the almost solitary argument that has emerged from the opponents of the trophoblast theory; but, as I say, it by no means states the whole truth, which has been quite well known for some time. As in the case of almost all the body ferments, trypsin has its precursor, which is called trypsinogen, and which was discovered by Heidenhain. This substance, and this alone, is found in the pancreas, and it has no action whatever upon proteids. If therefore an aberrant germ-cell had found its way into the pancreas, and some cause led to its development into trophoblast—“cancer of the head of the pancreas”—it would have no more difficulties there than anywhere else. On the other hand, the development of a tumor in the upper part of the intestine *would* have to reckon with trypsin: and tumors there are excessively rare.

The great Russian physiologist, Pawlow, has proved that whilst the pancreatic secretion, as it leaves the pancreas, is without any appreciable action upon proteids, it very rapidly becomes active when a small quantity of the intestinal juice is added to it. There has indeed been discovered in the intestinal juice a body which, by some means or other, converts the inactive trypsinogen into active trypsin. This body was called enterokinase by Pawlow, and he regarded it as being itself a ferment. Some French observers have disputed this, but according to Professors Bayliss and Starling, and Dr. J. M. Hamill more recently, of University College, London, Pawlow was right, and there seems to be no doubt that the trypsin which daily does invaluable digestive work within the bowel of each of us is itself a product of the fermentation of trypsinogen by the intestinal ferment enterokinase. It is well here to recall also the fact which was actually observed by Kühne,¹ that glycerin extracts of the fresh pancreas are of little or no digestive capacity, and require the influence of such a substance as dilute acetic acid in order to develop trypsin within them. This acetic acid has constituted a grave nuisance during the whole of the earlier stages of the pancreatic treatment of cancer, since it has occurred in most of the injections that have been put upon the market, and since, as might well be expected, it causes much pain when introduced under the skin. These facts regarding the secretion of the pancreas are of far greater moment, however, than any question of painful injections, for they bear immediately upon the whole theory of the relation between the pancreas and cancer.

¹Trypsin was discovered by Corvisart in 1858, and named by Kühne in 1876.

Some time ago it was shown that arrest of all the activities of the pancreas leads to the occurrence of the disease called diabetes, and some authors have supposed, though this is doubtful, that certain peculiar "islands" of cells found here and there in the gland produce a special substance which is absorbed into the blood, and by its continuous presence there prevents the occurrence of diabetes. If we ignore the recently challenged assertion that these special islands of cells have this special function, then the theory must undoubtedly stand as fact. There can be no question that the pancreas or some part of it does produce an "internal secretion," as the phrase goes, which serves to insure the proper performance of the bodily chemistry, a disturbance of which constitutes the disease diabetes.

But there is no definite reason to suppose that there is any parallel between the case of diabetes and the case of cancer in this regard. The product of the pancreas is trypsinogen, which is normally converted into trypsin in the bowel and does its work there—which is to complete the proteid digestion commonly begun in the stomach. It is not yet known whether the trypsin so formed ever returns as trypsin to the body. Probably in the course of the various decompositions that occur in the ordinary civilized man's bowel it is destroyed, but it is quite conceivable that this trypsin might escape destruction, and might actually be absorbed by the absorbent cells of the bowel, just as the nutritive products of the digestion of the food are absorbed. If this were so, the trypsin thus gained by the blood would have an antagonistic effect upon any trophoblastic or cancerous tissue with which it came in contact, until it was disposed of, probably by the kidneys. As we shall see, enormous doses of active

trypsin have been injected, in Warsaw, under the skin of animals. These were disposed of by the kidneys, the activity of the ferment being still retained—but the animals displayed no symptoms of any kind whatsoever. These experiments have been repeated and extended lately, with similar results, by Pinkuss and Pinkus in Berlin.

This last is an absolutely cardinal fact, and must be insisted upon in our study of the pancreas. I quote, for instance, from the article on "Therapeutics," written by a highly distinguished physician for the tenth edition of the *Eycyclopædia Britannica* (vol. xxxiii, p. 273): "The secretion of some digestive glands would prove poisonous if absorbed unchanged, *e.g.* the trypsin of the pancreas digests albuminous bodies in neutral or alcoholic solution, and if the whole of that which is secreted in the pancreas, for the digestion of meat in the intestine, were absorbed unchanged into the circulation, it would digest the body itself, and quickly cause death." This dogmatic statement is wholly untrue. On the contrary, it may now be positively asserted that trypsin has no action upon the cells of the normal body. Thus, when enormous doses of it are injected under the skin, they affect in no way whatever any of the normal tissues of the body, and if the body holds none but normal tissues, no results of any kind are to be observed; but if there be growing in it what we call cancer or trophoblast, *that* is poisoned by the ferment.

Whilst, on the one hand, we know definitely that the living pancreas never produces or contains any trypsin, and, therefore, cannot pass it into the blood directly, we know, on the other hand, that the trypsinogen which it pours into the bowel, and which is there converted into trypsin,

has its own work to do; and we do not yet know whether any of it ever gets into the blood. In the present state of our knowledge, therefore, it is very necessary that we should ascertain whether the blood of an individual whose pancreas is in perfect health and full activity ever contains any trace of trypsin.

So much for the later and longer period of the history of the pancreas; let us now consider its origin and earlier history. The pancreas arises from the innermost layer of the embryo at a very early stage in its history. As Dr. Beard showed in 1896 for certain of the fishes, the pancreas is formed and begins to function at the "critical period." Said Dr. Beard (*On Certain Problems of Vertebrate Embryology*, 1899): "It has been recorded that the pancreas in *Scyllium* begins to enter upon its functions with the introduction of yolk into the gut at the critical period. It is probable that the critical period marks the time in all vertebrates when this secretory structure first commences its functions." The activity of the pancreas is necessary for the digestion of the yolk, which at this period is drawn into the gut, "where, during the rest of the development within the egg case, and for some time afterwards, it serves for the nourishment of the young fish."

The positive evidence of pancreatic activity is obtained by the microscope, for it is at this period first that, when the cells of the gland were examined, they were found by Dr. Beard to contain the tiny granules which yield its digestive secretion. At the International Physiological Congress, held at Heidelberg, August, 1907, Barbera reported that he had examined the foetuses of dogs in various stages, and found trypsinogen produced by the pancreas and enterokinase by the bowel—the amount pro-

duced increasing with the development of the organs. We may note again that there is no digestion of food for the trypsin to accomplish in man; but there is digestion of trophoblast.

In the case of man, it is quite certain that the seventh week of development corresponds to the critical stage. It is at this stage that in man and the higher mammals generally, a change of the mode of nutrition is brought about by the suppression of the trophoblastic tissue. This tissue has been variously named, and is most commonly known to physicians as the 'syncytium' of the chorion. Prof. Hubrecht in 1899 gave it the name of trophoblast.

Now in the light of what we have already said regarding the way in which the pancreas does its work, those who care to go closely into this question will be inclined to ask how it may be supposed that the substances produced by the pancreas in its earliest stages can reach the trophoblast in such a way as to cause its digestion. It is now demonstrated that the foetal pancreas sends its trypsinogen and other ferments or their antecedents into the empty bowel; whence, in foetal life, at any rate, they may be readily absorbed into the blood. The trypsin which reached its perfect state in the bowel will pass through the kidneys and thence, as the embryologist will understand, to the allantois, or foetal bladder, in parallel with the case of the dogs observed by Pinkus. Having once travelled so far, the trypsin must obtain ready access to the trophoblastic tissue within which the allantois is developing.

If these considerations are correct, we should expect very marked and serious consequences to ensue in cases where, for any reason, the pancreas does not develop. Now this sometimes happens, as we have seen. There

are known cases in which the embryo undergoes defective development so that its pancreas is either never formed, or fails to perform its function. In such cases there is nothing to arrest the indefinite growth and multiplication of the cells of the trophoblast, and these accordingly go on multiplying. The consequent deadly form of malignant tumor is only too well known, and is commonly called chorio-epithelioma. I quote from Dr. Beard:²

“In human gestation, if at the critical period the embryo be wanting or very abnormal [a very abnormal human embryo can only persist as one of identical twins], the phenomena of the critical period are lacking, and the normal trophoblast, which always begins its life by eroding the uterine epithelium and wall, may go on with this process, exhibit indefinite powers of growth, and eat its way through uterus and other organs, finally blocking the lungs and brain of the mother. This is chorio-epithelioma, recognized to be a form of cancer by Prof. F. Marchand in 1895. This is without doubt the most deadly form of cancer. Here, the sexual generation being unable to suppress the asexual one, or trophoblast, the latter exhibits the characteristics of asexual generations, the powers of indefinite growth and increase.”

²“The Interlude of Cancer,” *New York Medical Record*, February 2, 1907.

CHAPTER VI

THE EVOLUTION OF THE DISCOVERY

IN the preceding chapters I have endeavored to trace in logical fashion the various parts of the theory upon which the new treatment of cancer is based. In the present chapter it is necessary very briefly to refer to the stages of Dr. Beard's work, especially because his right to priority has been questioned, directly or indirectly, on one point or another, both in Great Britain and in Germany.

Dr. Beard's published works show that, so far back as 1902, the work which he began in 1888 had led him to enunciate the conclusion that cancer is an irresponsible trophoblast (*Lancet*, June 21, 1902, p. 1758).

The problem as it then presented itself to Dr. Beard is thus expressed by him: "It was that in every normal development the trophoblast, which in the absence of a completed embryo might become a malignant tumor, chorio-epithelioma, was invariably suppressed and degenerated. The task was to find out how this came about. For there appeared to be good reason for the hope, if not for the sure belief, that the factor, or factors, which brought about this result in normal development might also be potent when directed against an irresponsible trophoblast or cancer."

On December 13, 1904, Dr. Beard read a paper before the Edinburgh Pathological Club.¹ This paper consti-

¹An abstract of this was printed in the *Lancet*, February 4, 1905.

tutes the first assertion of the solution of the cancer problem, and the first suggestion of the use of trypsin. In this paper Dr. Beard laid down the proposition that "The change in nutrition initiated at the critical period in vertebrate animals, from fishes to man, is based in the commencing functional activities of the pancreas. This introduces an alkaline digestion by means of the pancreatic juice with its various ferments. . . . Under the conclusions already advanced regarding the nature of cancer as an irresponsible trophoblast, in consideration of the facts regarding the acid and eroding action of the trophoblast and of carcinoma, and in respect of the fact that, in the absence of a completed embryo or foetus and its pancreatic secretion, the trophoblast may become one of the most deadly of malignant tumors, chorio-epithelioma, it must be clear that nature itself has possibly provided a remedy for cancer, and the pernicious [intracellular] cancerous digestion of the trophoblast, in the secretion of that important digestive gland, the pancreas. . . . Moreover, it is very important to note that, just as cancer is found everywhere in the vertebrates, just as there is one mode, and one only, of vertebrate development, so the pancreas and its secretion are a common heritage of vertebrate animals.² . . .

"Practically all that was sought after from my own researches, regarding cancer, has now come to light. Embryologically, the problem of cancer has been to discover the antithesis of two enzymes [ferments], and in particular to find out the enzyme capable of destroying a weaker one, and thus of leading to the degeneration of the

²As noted elsewhere, trypsinogen, enterokinase and trypsin have lately been proved identical in vertebrates generally by Dr. J. M. Hamill.

tumor by simple atrophy. The whole story is but another example of that antithetic alternation which underlies all the phenomena of living things. The solution of the problem of the functional relation of embryo and trophoblast, how the latter nourishes itself by an [intracellular] acid peptic digestion and degenerates slowly by a pancreatic digestion, becomes at the same time the embryological, if not the medical, resolution of the problems of malignant neoplasms, as well as of chorio-epithelioma. As an embryologist who is not a physician or surgeon my task is ended. The further applications of the scientific and theoretical solutions of the problem may safely be left in the hands of those who know far better how to employ it. But they may not forget that in nature the degeneration and disappearance of these asexual structures, sometimes quick, are often exceedingly slow, though sure. Not that it is likely that the surgeon has removed his last malignant tumor, but that, as one of the results of the work begun more than sixteen years ago, the physician has possibly had forged for him a light and not dangerous weapon, only second, if not equal, in potency to the surgeon's knife."

Elsewhere we shall see in what fashion the *Lancet* expressed its appreciation of the privilege of printing this paper, in which an unsurpassed discovery in the realm of rational therapeutics was first announced.

Only a few weeks after Dr. Beard's lecture, Dr. Shaw Mackenzie began the use of hypodermic use of trypsin in cancer, and to him, undoubtedly, must be awarded the credit of being the first physician to employ the new treatment. (For the date, January, 1905, see Dr. Shaw Mackenzie's book, *The Nature and Treatment of Cancer*, p. 4.) Dr. Shaw Mackenzie, however, bases his prac-

tice upon a theory of his own regarding the nature of cancer, and uses trypsin in the belief that there has been demonstrated its power of breaking up the substance called glycogen. It is hardly necessary, however, to say that trypsin has no such power. There is no known ferment which affects both proteids and carbo-hydrates, such as glycogen, and to any student of the ferments in general (see Chapter IX) it is inconceivable that there should be.

It is interesting to go back a little further. In the *Lancet* (June 21, 1902), Dr. Beard had stated that the substance which would destroy cancer must be contained either in foetal blood or in the allantoic placenta. In December, 1904, knowing that cancer occurs lower than the mammals—or placental animals—he could exclude the placenta; for the degeneration of trophoblast occurs in all the higher animals and not the mammals only. In that month, in controversy, Dr. Beard remarked that “the mammalian embryo solved the problems of cancer ages ago.” To see this phrase in print was to suggest to him the need of turning back to his early work on the critical period. My purpose is to illustrate the conditions under which discoveries are made, and I will here quote from a private letter of Dr. Beard to myself:

“At once, December 8, 1904, I got out all my critical period preparations in this room, as well as my paper on the critical period. I looked at some of the slides of post-critical embryos, especially at the digestion of yolk, then at my paper, and saw at once that I had neglected to lay stress, as a character of the critical period, on the commencing functional activities of the PANCREAS-gland. So the problem was solved so far. The other thing is a later story. At once I saw there must be an antithesis of ferments, but was not aware whether any ferment had been described in the cancers. But I postulated the existence of an intracellular ferment therein, acting in slightly acid medium. I set about

getting chick blastoderms, as I could get no fresh cancers. Then I recalled that HARTOG³ had already described such a ferment in chick blastoderm of three days. In the meantime I had tried to get out from the Univ. library Hoppe-Seyler's big book on physiological chemistry. It was out, so I had to wait for it. It came about four days before my lecture in Liverpool was due. In it I found the reference to Petry's paper. Next day, January 18, 1905, after lecture I went and got out the vol. of the *Zeitschr. f. Physiol. Chemie* with Petry's paper. Opened it in the library and read it in going along the Quad. to my room. Then it was you might have heard my heart thump. All was exactly as I had foreseen. The cancers had a ferment acting in acid medium, and as they had no ducts, it was intracellular, its intracellular nature being afterward stated by Blumenthal."

This letter was not sent me for publication, but I have taken the liberty of putting it on record for its personal and general interest.

³The reference is to Professor Hartog's paper, "Some Problems of Reproduction," *Quarterly Journal of Microscopical Science*, 1904, p. 583.

CHAPTER VII

THE IMMEDIATE CAUSES OF CANCER

THE PREDISPOSING CAUSES

IN the study of the causation of disease, we very commonly find it convenient to divide such causes as we can recognize into two categories—the predisposing and the exciting. Thus, for instance, in the case of the most fatal disease of all, consumption, we say that the predisposing causes are such things as long exposure to foul air, while the invariable and essential exciting cause is the tubercle bacillus. If we apply this terminology to cancer as we now conceive it, we discover that in this case, according to the theory of Dr. Beard, the predisposing cause is a constant thing, the presence of an aberrant germ-cell having definite possibilities, while the exciting cause or causes are not elucidated by his work. In point of fact, though students of disease commonly accept these terms, there is no philosophic defense for them. In this complex universe causation is complex, and there is no one cause of any one thing. The universal past is the cause of any one event. Still we may take it that the presence of an aberrant germ-cell of a particular kind is the predisposing cause of any malignant growth, and this preliminary proposition requires brief comment.

It is the observed fact of the development of certain

of the lower animals, as discovered by Dr. Beard, not only that aberrant germ-cells can be detected in various parts of the body, but also that they are most commonly seen in those sites—such, for instance, as the mouth and the stomach—in which human cancer is most commonly known to arise. This fact in itself lends support to Dr. Beard's theory, in which we recognize, so far as this part of it is concerned, a new form of the view long entertained in various forms by many students, that the cells from which a cancer arises have always been from the first essentially different to the other cells amongst which they lie. The theory of Cohnheim, for instance, asserted that cancer arose from cells which properly belonged to one layer of the embryo, but had lost their way and become lodged in another layer. Various surgeons also, without any more specific statement, have inclined to the view that some local peculiarity is always necessary for the excitation of cancerous growth.

Directly we consider the causes which are known to excite cancer, we find evidence which seems to support this view. It is known, for instance, and is disputed by no one, that cancer on the edge of the tongue can often be traced, quite definitely, to the irritation of a jagged tooth, and cancer of the lip to that caused by smoking a hot clay pipe. But to take the first instance, do we sufficiently recognize a fact which has always puzzled myself, and which no surgeon, I think, would question, that for every one case of cancer of the tongue resulting from the irritation caused by a jagged tooth, we should be able to find scores or hundreds of cases in which similar irritation produced nothing but a simple ulcer, which rapidly healed when the cause was removed? Or again, to take the case of cancer of the lip, if every

one who smoked a clay pipe doomed himself to cancer, the fact would be familiar, and the habit would have been abandoned long ago. But similar causes do not produce similar effects in this instance—which is to say, of course, that these causes are not all the causes. Of a hundred smokers one will contract cancer and the others will continue to smoke with impunity. Something is present in him, or lacking in them, which determines the difference. These facts, which might be multiplied indefinitely from cases of local irritation in any part of the body, lend very strong, though of course not conclusive, support to the theory that before the exciting causes of cancer can be operative, it is necessary that there be a particular capacity for reacting to them in the part in question, and this capacity may be most readily attributed to the presence in it of cells of a special kind. The facts do not lead to anything more definite than this; of course, so far as they are concerned, the cell may be an embryonic cell or a germ-cell. It is for other facts to determine whether a germ-cell alone can be conceived as giving rise to the kind of tissue which we recognize in malignant growths.

We may consider yet another fact, which must puzzle the more thoughtful among medical students when they first make their acquaintance with clinical surgery. It is very well known to be the all but invariable rule that cancer of the lip is found in the lower lip and not in the upper lip. Many a surgeon who has operated upon hundreds of cases of cancer of the lower lip has never seen a case of cancer occurring in the upper lip. Yet if we consider the smoker, it is very difficult to see why this should be so. We should expect, I think, more often than not to find cancer starting at opposite places in the two lips simultaneously, or perhaps a little later in the

upper lip. Yet this simply does not happen. Would not the inference appear to be that there is something present in the lower lip, or absent in the upper, which is necessary for the production of cancer? Now any one who will study the embryology of the face and compare the mode of development of the two lips will readily believe that it must be vastly easier for an aberrant germ-cell in the course of development to find its way into the lower lip than into the upper lip.

These considerations are not to be ignored, I think. Yet at the same time, and with all due deference to Dr. Beard, it seems not wholly inconceivable that sometimes even a somatic cell—that is to say, a cell of the body proper—might undergo such reversion as to become not, perhaps, a true germ-cell, but a cell capable of giving rise to trophoblastic tissue. It would be absurd to assert that this positively occurs, but it would be difficult to assign any reason why it can never occur. Our ignorance of the interior processes of cell life is abysmal. Though we find characters fundamentally identical in all cells, whether a tubercle bacillus or the brain-cells of some genius like Spinoza or Schubert whom that bacillus destroys, we can only conjecture as to the character of the interior processes, which, for instance, determine the specific inability of a brain-cell to divide, or the limitless capacity for multiplication displayed by a microbe. We observe certain results, but we are utterly unable to express their causation. It may be that a cell of the normal body—that is to say, a somatic cell—has forever left the high-road, along which life marches in its successive generations. Nowadays we conceive the individual and the cells which compose him as transient lateral off-shoots doomed to die, and serving merely as the host for the

deathless line of germ-cells. It may be then that a somatic cell is in a *cul-de-sac*, yet it is not inconceivable that within such a cell there remain potentialities which were proper to its remote cell ancestors. It is not inconceivable that even a somatic cell, under certain conditions, may give rise to trophoblast. I, for one, would not care, therefore, roundly to deny that pathologists are mistaken when, as sometimes, they seem to detect a continuous and multiple transformation of many cells proper to a part, into cancerous cells.

These questions are of the greatest biological interest, and of even great immediate interest, in relation to the study of the production of cancer. Yet, however they be answered, the answer does not affect us in practice, if the tissue of a cancer or any malignant growth be always trophoblastic, however derived; and, being trophoblastic, must necessarily succumb to the specific poison of trophoblast, which is trypsin.

A further question which we must here consider is whether or not heredity is of importance in predisposing to cancer. This is an extremely difficult question to answer in a dogmatic fashion. That heredity does predispose to this disease is the general belief of the medical profession and of pathologists. Numerous striking instances in special families are on record. Too much importance must not be attached to the fact that Prof. Karl Pearson, studying certain statistics, has pronounced them incapable of proving that cancer is inherited. As to those statistics his opinion may be accepted, but in all such cases it has to be remembered that the conclusion arrived at by the statistical expert is of just so much validity, neither more nor less, as the actual data from

which the statistics were compiled. It may be pointed out further that the theory of Dr. Beard certainly lends probability to what has so long been believed. Dr. Beard himself is quite convinced that this general opinion is correct, and that there is such a thing as the transmission of a predisposition to cancer. Needless to say, such a transmission is capable in various ways of agreement with the theory in question. It remains, of course, to inquire whether it depends upon the inheritance of a special liability to wander in the case of the germ-cells, or, on the other hand, upon the inheritance of such bodily conditions, whatever they be, as will favor, or permit, their untoward development in later years. But, at any rate, amongst the predisposing causes of this disease we must in all probability reckon with something which is capable of transmission by heredity.

The inadequacy of our category of causes is shown when we come to consider the case of the pancreas in this relation. Not a few diseases are known which are due to the occurrence of defect in the working of some gland. Instances are furnished by such diseases as cretinism and myxœdema, due to thyroid insufficiency; Addison's disease, due to suprarenal insufficiency; and diabetes, due to pancreatic insufficiency. It is upon the analogy of such diseases that Dr. Shaw Mackenzie has based a theory of cancer which states that the disease is due to failure of the pancreas. The tendency to its occurrence in later years suggests that the pancreas "gives out," so to speak, before the rest of the body—cancer follows upon senility of the pancreas. In the absence, so far, of any substantial evidence for this view, and in the presence of a host of facts which can scarcely be reconciled with it, we need not here discuss it further.

It obtains its chief interest from the fact that Dr. Shaw Mackenzie associated with it a special relation between cancer and the carbohydrate substance called glycogen, and that, under the erroneous impression that trypsin digests glycogen, he advocates the use of trypsin in cases of cancer.

In the light of Dr. Beard's work, however, we certainly seem compelled to seek a clear answer to the question whether the malignant development of an aberrant germ-cell may not be due, in some cases if not in all, to failure on the part of a previously efficient pancreas. In other words, are we to conceive the facts in some such manner as follows. That any, or many, or all, of us may possess, in various parts of the body, aberrant germ-cells which are such that if they develop at all they will develop into malignant tumors; that this development is normally prevented by the activity of the pancreas, which keeps the body sufficiently supplied with trypsin to prevent it; that if this supply fails from whatever cause, a cancer will probably result. These questions have yet to be answered.

I am well prepared to believe that the question of the absorption of trypsin from the bowel may possibly yet prove itself to be of great practical interest. The overwhelming difference between the bowel of the fœtus and the bowel of the independent individual is not so much, I think, that the one is functioning and the other is not, as that the one is microbe-free and the other is microbe-crammed. Microbes have been identified in the bowel of the baby so soon as eleven days after birth, and thereafter they never leave it. At this moment the bowel of every civilized being, with the very rare exceptions to which I am about to allude, contains unthinkable billions of microbes. Now these live, of course, by chemical

processes, and their activities profoundly modify the whole chemistry of the bowel. The reader will readily understand that the chemistry of a microbe-free bowel would differ incalculably from the usual case. So radical is the difference that I would suggest as at least credible a totally different fate for trypsin in the two cases. Now a remarkable and original student of digestion, Mr. Horace Fletcher, the well-known author of *The A B-Z of Our Own Nutrition*, has instituted a series of inquiries which show at least that, whether this bacterial condition of the bowel be normal or not, at any rate it is possible to be without it, and to flourish exceedingly in mind and body withal. We must admit as a proved scientific fact that it is possible to live and flourish, even to the extent of arduous athletic exercise and arduous intellectual exercise, upon what is really only a minute fraction of the food commonly consumed by civilized man. On Mr. Fletcher's principles this food is most rigorously masticated—so rigorously that there really is no time to eat any but very small quantities. Now the bowel under these conditions would seem to be an entirely different place, so to speak, from the bowel of the ordinary man. The "normal" large intestine—if it be rightly called normal—is the seat of continuous microbic decompositions of the most complicated and aggravated character. In cases of constipation the poisons thereby set up produce notorious effects. But what would constitute for us constipation so extreme as to be desperate, and suggest the necessity of immediate surgical intervention, is for the Fletcherite his normal and untroubled state. I hope I have not sacrificed explicitness to elegance in putting the facts thus. Now it seems to me to be perfectly credible that the Fletcherite bowel, which is practically

microbe-free, may differ from the ordinary bowel in this respect among others—that, like the bowel of the foetus, it permits the absorption of trypsin, whereas the ordinary bowel prevents its absorption by insuring its previous destruction. The fact that the pancreas produces zymogen granules, the precursors of trypsin, during several months of foetal life, is a demonstrable fact which any one can observe for himself under the microscope. Confirmed by Barbera's recent work, it is impossible to question that fully formed trypsin is made in the foetal bowel, when there is absolutely nothing whatever for it to do *in the bowel*; nor is there any difficulty in understanding that its absorption from the foetal bowel will be easy and rapid; whilst Dr. Beard has assigned to it a *rôle* momentous enough indeed. Now I submit that the Fletcherite bowel, which at its fullest is practically empty, and at its most septic is practically microbe-free, approximates so nearly to the condition of the foetal bowel, that if the absorption of undestroyed trypsin is credible in the one case it is credible in the other.

All this, of course, is speculation, but it is speculation perfectly capable of verification, and I submit that while it is not unreasonable in itself, there are certain facts which are in consonance with it—certain facts indeed, which by this speculation may be explained. In a word, I suggest that in many cases the absorption of trypsin from the ordinary bowel of civilized man is practically or wholly impossible; that, however, it is possible in the case of the bowel of the Fletcherite; that, as judged by results, the Fletcherite, and he alone, may be considered the wise and healthy eater, while the rest of us most grossly over-feed ourselves. It may be, then, that the very large number of facts which seem to show an

especial incidence of cancer in the well-to-do—that is to say, in the most grossly over-fed classes—the facts which show that it is especially a disease of man as against the lower animals (in whom, *except when domesticated*, it is extremely rare) and the facts which show that it is especially a disease of civilized as against savage man—are all capable of rational and scientific explanation in terms of the hypothesis which I here venture to advance.

It has been frequently asserted, and is still asserted, that cancer is a disease of over-nutrition; the body, being excessively supplied with nourishment, is liable to over-growth, which may take the form of cancer. That as it stands is a crude and evidently ridiculous theory, entirely failing to reckon with the wholly anomalous character of the so-called over-growth in question; but, on the other hand, it is possible to suggest that the three series of facts already named, which seem to associate cancer with over-nutrition, really mean that the person whose bowel is persistently filled with microbes and filth is thereby prevented from absorbing into his blood the trypsin which is produced in his bowel, and loses the preventive influence which that trypsin might otherwise exercise upon the development of cancer.

Needless to say, I am prepared to abandon this speculation the moment that it is disproved. If, for instance, the incidence of cancer among Fletcherites can be shown to be as high among other people, then I have nothing more to say. Meanwhile I submit that it is possible to state a reasonable case, which provides a new argument against over-eating, graver perhaps than any hitherto adduced.¹

¹See also p. 202.

CHAPTER VIII

THE MICROSCOPIC STUDY OF CANCER

HE would be a very fool, of course, who denied the magnificent and wholly indispensable part which the microscope has played in the advance of medicine and pathology. Without the microscope we could not have the cellular pathology, or cell-theory of disease, not the least important teaching of which is the universally admitted cell-theory of cancer. It is also impossible to deny that the microscopic study of cancer has quite lately accomplished excellent work, as, for instance, in the proof of the not infrequent occurrence among the cells of some cancers of the peculiar type of division which had previously been regarded as exclusively characteristic of certain stages in the history of reproductive tissue. Great interest and significance also attach to the recent microscopic demonstration by Schmidt of the fashion in which the fluid part of the blood is enabled to inclose, and subsequently to kill, cancer-cells which have just dissolved or digested their way through the walls of the blood-vessels. It may be suggested that trypsin is the agent here, as indeed in the positive cases of the spontaneous cure of cancer.

But it is not too much to say that there is an all but regrettable aspect which the microscopic study of cancer presents to us, as Prof. von Leyden observes in the important paper in which he announces his adherence to

the theory of Dr. Beard that trypsin has a specific, selective, digestive action upon certain constituents of cancer-cells. He there comments upon the fact of the very long period, amounting to something like half a century—a period now happily forever closed—during which the study of cancer has been carried on as a study in minute anatomy. Morphology being the science of form, we may say that until this present, or rather until the work of Dr. Beard broke new ground, the study of cancer has been morphological—that is to say, a study of the appearances found under the microscope. The initial discovery of the microscope in this respect, the discovery that every malignant tumor consists in the growth of cells peculiar to it, and antagonistic to the normal cells of the body, was of course a fundamental and essential one, constituting, indeed, the first great epoch in the history of the subject.

But what do we find? The facts, indeed, demonstrate what is so lamentably familiar to the student of science. A new method is introduced by some great pioneer, a Virchow or another; then for a long period innumerable students, endowed with honesty and perseverance no doubt, continue to prosecute this method—not without results, of course. But there is a limit to the fertility of any scientific method, and the trouble is that the method which has proved its worth becomes a fetish to its prosecutors, and no really substantial advance is made until another genius arises with a new method. The solution of the problem of cancer as a problem in morbid embryology is a splendid case in point. The further solution of the problem of its treatment as a problem in specific cell chemistry is yet another.

Let us now see how jejune have been the usual investigations of cancer by the microscopic methods. All over

the world the young student, introduced to the subject of malignant tumors, has his attention directed by his pathological teachers almost exclusively upon the question of minute anatomy. True, he has learned in the laboratories of physiological chemistry that cell behavior is a matter of cell chemistry. True, also, if he reads Herbert Spencer, he has learnt that function precedes and creates structure, while it is an elementary fact of physiology that, though all liver cells are exactly alike, yet the organ which they compose has at least half a dozen distinct and classifiable chemical functions. Yet for all that, the trouble is that the academic pathologist is essentially a man of the microscope, and, therefore, there is no pathology for him but what his microscope reveals. This is not a peculiarity of the pathologist. It is only the consequence of the law of the mind, which shows itself in the musician, the party politician, the cook, or any one else. But it is dissonant with the facts of nature, which are more various than is dreamt of in the philosophy of any specialist of any order.

Look up the text-books, and we find page after sterile page filled with what? Not the function of the cancer-cell, which is everything, but its structure, which according to all the laws of biology is nothing but a labile modification, created by the function as its servant. Hence this is why Sir William Collins was so profoundly right when he said, long ago, that we must learn from the Spencerian principles of cell life, if we would solve the problem of cancer. Hitherto the medical student spends weary weeks at home and in the laboratory in order that he may learn at a glance how to distinguish a section of a spindle-cell sarcoma from a section of a round-cell sarcoma, a glandular epithelioma in one organ

from one in another organ, and so forth. These things will be shown him at his examination, and he will pass or fail according as he can or cannot name them. But the names matter not at all. Spindle cell or round cell, they both kill. If they both kill, it is not the round cell that kills because it is round, nor the spindle cell because it is a spindle (as a matter of fact these terms do not even correctly describe their shape), and, therefore, their shape is demonstrably a matter of no moment. If they do not kill because of their shape, let us hasten to the serious question, which is, Why do they kill? In other words, five seconds' study under the microscope of any two different sections of malignant tumors demonstrates to any one who will think at all that this is not the method which will ever lead anywhere. All that the microscope can reveal is difference of cell shape; all that matters a straw is identity of cell action, which the microscope can never see. But the student learns from one teacher that malignant tumors are divided into these, those and the others. However, he is to be examined by another teacher, whose text-book states a different division. His eye travels over acres of prints and notes, trying to find out how malignant tumors are divided. Thousands of students all over the world are doing this at this moment; but it does not matter a straw how malignant tumors are divided. The only thing that matters is how they are united. They are united because they are malignant, and they are malignant because of what they do. This microscopic study of cancer is very much less rational than would be the choice of a Prime Minister or an orchestral conductor by the cut of his clothes. A man usually puts on his clothes in order to keep countenance with his company; so does

the malignant cell change its shape, but not its essential malignancy.

As the question about a man is, What is he, and what does he? and not, Does he shave his chin? so the question about the cancer-cell, which medical science has practically ignored for half a century, is, What is it, and what does it? and not, What does it look like? It is not possible, by the microscope, and never will be possible, as our knowledge of the limits of microscopic vision tells us, to see the inner shrine of the temple of life. The ultimate vital processes are forever hidden from the eye of man. The microscopic stage of pathology in general, and not only of the study of cancer, was a necessary and invaluable one, but it must yield to something deeper. To my mind, the analogy with astronomy is amazing. No one will decry the telescope. Modern astronomy could not exist without it, any more than modern pathology without the microscope. But there came the point at which the fertility of the telescopic method was practically exhausted. It could, can and will go on indefinitely adding in quantity to the same kind of knowledge as that already attained by it. Similarly the microscope will go on adding to the same kind of knowledge as that already gained by it. But if you desire a new kind of knowledge you must introduce a new method. In astronomy that method is embodied by the spectroscope. The telescope can see a distant star, but the spectroscope can enable the mind's eye to see the structure of the atoms in that star, which the bodily eye could not see, however near to it they were. The introduction of the spectroscope has created a whole new astronomy to which the whole preceding astronomy was merely a matter of finding out our whereabouts and obtaining mate-

rials for study. The introduction of bio-chemistry, as it is called, its instruments the instruments of the chemist, is about to work a similar revolution in the whole of biology, including morbid biology, which we call pathology. Just as the telescope could go on finding out new stars indefinitely, but could never tell us what they really were, so the microscope may go on indefinitely finding out new shapes of malignant cells. I should say that the shapes of these cells are probably potentially infinite, which is apparently more than can be said of the stars; but in order to find out what these cells *are*, the only thing that matters, a new method is necessary. Dr. Beard began by introducing the historical or embryological method, and upon it he based a conclusion as to the specific relation of trypsin to the malignant cell—a conclusion which might, or might not, prove to be identical with the conclusion of yet another method—the chemical or bio-chemical method. As Prof. von Leyden puts it, the question really worth asking now is whether there are specific substances peculiar to malignant cells. All malignant cells kill, whatever their shape. It is this killing that concerns us who are killed. In this they agree with each other and differ from all non-malignant cells. Von Leyden's question, then, can be answered without further inquiry by the use of pure ratiocination. It is a logical necessity that there must be such specific substances, whilst it is evidently extremely probable that, indeed, they will be found to be one group of such common to all malignant cells.

The next question is whether it is possible to produce a specific destruction of such substance or substances: and if they are essential to the life of the cell it will die. We know now that there is such a substance, and that

under certain conditions trypsin destroys it. Nothing could be simpler. No line of inquiry could now seem to be more clearly indicated for the student of cancer, yet look up the text-books of pathology, and see what we find about it. If ever there was an illustration, here, indeed, it is, which vividly expresses the biological truth that function precedes structure, which is no more than its creature and servant. Furthermore, just as you may change your servant or your attire, which is an inanimate servant, according to your needs, so the functioning cancer-cell, whose interest it is to live, and not to make itself circular, or spindle-shaped, or parallelopipedal, or anything else in particular, will assume any kind of shape—not infrequently in imitation of the tissues among which it finds itself. This microscopic examination has grossly deceived all but the very few pathologists. Conceive yourself as a man with a microscope, who runs the grave risk of having his inner as well as his outer vision limited by the microscope. You see malignant cells lying beside cells normal to such a gland as the breast. The two sets of cells look very like one another. Perhaps it is only the misplacement of the malignant cells which distinguishes them *to your eye*. You conclude, therefore, that this misplacement is the essential phenomenon. How many gallons of ink have not been spent over this idea of misplacement as constituting the real distinction.

But if you are wise, even as you gaze down the microscope, you will keep firmly before your inner vision the capital fact, which what you see there tends to obscure—the fact that the normal cell and the malignant cell next it, though they look like brothers, are fundamentally and essentially not so. What fact, indeed, could more clearly indicate the subordinacy of structure than this fact which

every pathologist knows? It is universally admitted by the pathologists that they cannot tell a single cancer-cell to be a cancer-cell. The most they can go by—and they are frequently wrong, as every clinician knows—is simply this question of the invasion or misplacement which the growing edge of a tumor may show. Yet in face of the fact that of two cells which cannot be told apart nor even together, one may be a normal cell of the body, while the other—and no one can say which is which—is an enemy of the whole body, and will certainly kill and destroy the first; in face of the fact, indeed, that the two cells differ as widely as any cells can differ, for there is no cell difference more extreme than that the life of either should mean the death of the other—in face of this fact the microscope fetish is still worshipped. Monstrous at first sight may appear Dr. Beard's assertion that these two apparently identical cells actually belong to different generations in the animal life-cycle, yet what assertion of their fundamental difference can possibly demonstrate it more clearly than the familiar facts of their actual vital relations to one another?

Misled by appearances, the pathologists teach that the malignant cell is simply one of the cells of the part, which differs in having taken on powers of unlimited growth. Nothing is more commonly repeated about malignant tumors than this. But unlimited growth as such is not peculiar to the cancer-cell, and if it differed in nothing but this, cancer would not be cancer. It is the innocent tumor, the harmless fatty tumor, for instance, that displays exactly what pathologists assert to be the *differentia* of the malignant cell—power of unlimited growth. The cardinal fact about the malignant cell is not that it grows indefinitely, though that is true, but the fact that

it grows by killing the normal cells and destroying normal tissues, which is exactly what the cells of a fatty tumor, with their power of unlimited growth, never do.

In a word, the only thing really worth seeing in a cancer-cell, the something by which it kills, is precisely that which the microscope can never see.

CHAPTER IX

LIFE AND FERMENTATION

DOUBTLESS the microscopist is not wrong in his assumption that the minute anatomy of cancer would tell us much that it vitally concerns us to know. But the anatomy that really matters is molecular, and almost infinitely more minute than the most delicate features which the present microscope or any future microscope can discern. In the next chapter I shall discuss certain general considerations regarding the chemistry or molecular anatomy of cancer, following in this respect the greater part of Dr. Beard's latest paper:¹ whilst the more immediately practical aspects of this question—which we have already seen to be the fundamental question of cancer—will be discussed in the chapter wherein, for the convenience of the serious student, I consider as a whole the recent German contributions to this subject.

Meanwhile it is desirable that we should study certain general facts as to the relation between life and fermentation. These will enable us to see that the subject of fermentation goes to the very basis of the structure and function of all living cells whatsoever: and it may become evident as a necessary truth that in fermentation, and in that alone, we have the key to the control of vital processes in general, whether in order to arrest or facili-

¹In passing this page for press, I learn that this paper appeared in the *New York Medical Record*, Oct. 19, 1907.

tate or direct them. There is no question as to the universal importance of the subject, quite apart from the problem of cancer.

It has frequently been declared that life itself is nothing but a series of fermentations. It is now believed that the stimulant action of the sperm in initiating development is that of a ferment. Yet again, it is fermentation that produces alcohol, with its incalculably malignant consequences; and lastly, the action of a ferment is in itself so wonderful a thing, and so closely suggestive of the behavior of a living creature, that the student of the nature of life might well spend the brief span of his own life upon this subject alone.

Men have known for long ages that if something called yeast be added to a solution of sugar there is a disturbance in the fluid, with the production of gas and bubbles and froth, and of alcohol; but the matter was not understood.

In the early part of last century, however, the great German chemist, Liebig, formed a theory as to the causation of fermentation, not to mention the putrefaction which is going on everywhere, and this we may call the chemical theory. There must be certain substances called ferments which, by some chemical property, excite these striking and vastly important processes.

Then there arose a chemist yet more illustrious, the Frenchman, Louis Pasteur, and he, fortified by the newly discovered fact that yeast is a living creature, denied altogether the chemical theory of Liebig, and produced a large number of facts which seemed to show that all fermentation and putrefaction are the work of living creatures. These it contented him to call microbes, as a comprehensive and not too precise term. This was a

vital theory of fermentation, as opposed to the *chemical theory* of Liebig, and it was admitted on nearly all hands that Pasteur was right and Liebig wrong.

However, there were discovered the digestive ferments, such as pepsin, with the name of which we are all familiar, while trypsin was discovered in 1858, very nearly half a century ago. Now these substances are not living cells. Furthermore, we now know that alcoholic fermentation is immediately produced by a non-living ferment which has actually been extracted from the bodies of the yeast-cells. There are, then, many ferments which are not alive, but these are produced in and by living cells—yeast-cells, the gland-cells of the stomach, the pancreas, the salivary glands, and so on.

Each of the two great chemists had half the truth. Pasteur was right in his assertion that fermentation is due to life. Liebig was right in his assertion that fermentation is a process due to the chemical action of lifeless chemical substances. We enter into and profit by the labors of both great controversialists.

At present we commonly speak of organized ferments and unorganized ferments, meaning thereby living ferments in the first place and not-living ferments in the second. This is a thoroughly unfortunate manner of speech, which should best be dismissed. If it were to be persisted in we should have to call every living cell an organized ferment, for every living cell produces fermentation. It is probable that even the fundamental act of breathing, the taking in of oxygen and the burning up of food with it, is controlled by a respiratory ferment—and every living cell must breathe or die. I shall entirely confine the word ferment here, therefore, to those chemical compounds—which it would be absurd to call

unorganized, since they are so highly organized that we can only guess at their structure—which are the immediate cause of fermentations; and we may begin by asking ourselves, in general, what a ferment is.

Ferments in general are very complicated chemical compounds, produced by living cells for their own purposes, and acting in the dissolved state in water—liquid water being found in all living tissues. But it is quite possible to obtain ferments in the dry state; trypsin, for instance, may be obtained as a mere whitish-yellow powder; it may be kept in this state for long periods, and after being dissolved again *may* retain some of its activity. Every one is familiar with pepsin in the form of a powder or even a tablet. The number of ferments is, perhaps, necessarily as large as the number of the varieties of animals and plants, but in general they answer to this description. It is probable that trypsin is a highly complex proteid or albuminous substance, of the class called colloids, and it is a typical ferment. All ferments are very sensitive to changes in temperature, and all of them, when dissolved in water, are rapidly destroyed at the very moderate temperature (60-65° C.) at which proteid or albumin, such as white of egg, becomes solid. Ferments in certain states stand low temperatures extremely well. It seems to me that this is a very interesting fact, if we remember that microbes will stand the temperature of liquid air for weeks. Sunlight rapidly destroys most ferments, and so do such familiar substances as hydrochloric acid. Since this is the digestive acid produced by the stomach we may readily understand that pepsin is a conspicuous exception to this rule, and acts most vigorously in the presence of a quantity of

hydrochloric acid which would instantly destroy practically all other ferments.

From the chemical point of view, perhaps the most remarkable fact about the ferments, in general, is the extreme simplicity of the means by which they produce results so potent that without them there would be no life upon the earth. We may practically say that all ferments either add oxygen to other substances or take it away, or add water or take it away; that is all. Meanwhile the ferment itself—and this is the capital fact—remains unchanged. While it is producing the most extraordinary results, changing the face of the earth, itself remains unchanged and loses none of its power. Its mere presence suffices. This, of course, is the standing puzzle about which chemists have been puzzling their brains for three-quarters of a century, and it constitutes the essential difference between ferments and the powerful chemicals with which we are all familiar. Strong nitric acid will do big things, but a given amount of nitric acid will only do a given amount of work, and it is utterly destroyed in the process. The amount of work which can be done by the millionth part of a grain of a ferment is absolutely and literally infinite. This is one of the greatest facts in the whole realm of science if it be properly considered.

Now if it be that the chemical actions induced by ferments are so extremely simple, why should they be of so many different kinds? Our digestive apparatus alone, quite apart from the rest of the body, produces ferments the number of which may probably be reckoned by the dozen. Why should there be so many different kinds of ferments, all capable of doing only the same

thing, such as causing other substances to part with their water or to take water in?

The answer, and it is a most important one, is that though a hundred different ferments may all do just one and the same thing, there may yet be only one substance upon which any one of them will act. This fact we may call, to use technical terms, the specific nature of ferment action. Prof. Emil Fischer of Berlin, far and away the greatest living student of organic chemistry, now that the illustrious Berthelot has departed, has studied this question, and he has actually shown that of two substances identical in composition and in every character—except that they differ in structure as your left hand differs in structure from your right—a given ferment will act upon the one and not upon the other. As Fischer puts it, the ferment and the substance to be fermented must fit like key and lock, or nothing happens at all. The reason why the number of ferments or keys is countless is evidently to be found in the number of different locks that have to be opened. Fischer's extraordinary discovery, to which I have alluded, reminds us of the first discovery made by Pasteur himself, who showed that certain kinds of microbes ate up and destroyed—that is to say, fermented—particular solutions of sugar made up of what we may call right-handed molecules, but had no action upon other solutions absolutely identical, except that the molecules were, so to speak, left-handed. Such great advances has Fischer made that in many cases he can actually predict from the structure of a substance whether a given ferment will attack it or not—that is to say, what particular key will fit a particular lock.

These facts are interesting from many theoretical points of view, but here we must specially consider their

bearing upon the new discoveries regarding cancer. According to Dr. Beard, looking at the matter entirely from the biological point of view, trypsin is capable of digesting certain substances necessary to the life of the cancer-cell, but has no action upon the corresponding substances which are found in the healthy cells of the body. The German workers have exhaustively proved this by experiment, as we shall see. His theory exactly fits in with what the chemists have taught as to the nature of ferments. The substances characteristic of a cancer-cell may differ from those characteristic of a body-cell only just so much as your right hand differs from your left, or as the drawing of a knife differs from that drawing seen in a mirror. Yet even if the difference be no greater than this, the theory that trypsin should attack the one, but not the other, is perfectly consistent with everything that the chemists have taught us about ferments. Those who have criticized this part of the theory on account of its improbability would have praised it as reasonable and probable if they had taken the precaution of first acquainting themselves with the elementary facts of the ferments.

But the immediate object of this chapter is to present to the reader the facts of fermentation in general, and I must pass on at once to mention the existence of certain perfectly simple inorganic substances which are also capable of producing fermentation. Even as long ago as the time of Faraday, it was discovered that such a substance as platinum is capable of causing what cannot be distinguished from fermentation—and this more especially if the platinum be finely divided, as in the case of platinum black. Some idea of the power of these substances may be gained from the fact that the action of one-three-hundred-thousandth part of a milligramme of platinum

“upon more than a million times its weight of hydrogen peroxide” could still be detected. Now a milligramme is a thousandth part of a gramme, and that is only fifteen grains. We get into very deep waters when we begin to study, as we may, the fashion in which poisons, such as prussic acid, will arrest this action or retard it; and we begin to ask ourselves whether the poisonous action of prussic acid upon ourselves is not simply due to its arrest of certain fermentations which are necessary for our lives.

For, indeed, it seems to be true that life is a series of fermentations. The reader will observe that I am not making any nonsensical statements about the supreme fact called mind. The physical fact called life, however, does indeed seem to consist of a complicated chain of fermentations, and to be carried on by means of ferments. As most of us know, the whole system of life-processes on our planet must be traced to the wonderful activity of the green matter of plants, and in all probability we must look upon that green matter, which is called chlorophyll, as the first and greatest of ferments, which makes possible the existence of all other life and all other ferments. Abolish the green plant, and every animal upon the planet must die, whether it be called worm, or fish, or man. In the last resort we are all vegetarians, every mother's son of us, whether we consume grass directly or the ox that consumes the grass.

More than this, all our most intimate and necessary vital processes are now seen to depend upon fermentation. Absolutely the most fundamental process of all life is breathing, and there is definite evidence to prove the existence, as I have said, of a ferment for this purpose. The next most fundamental vital process is diges-

tion, and all digestion whatsoever is nothing else but fermentation.

Furthermore, not merely do the processes of all life depend on ferments, but there are certain ferments of very humble kinds without which the earth would soon become a vast charnel-house. Putrefaction is not a pretty word, and the process is not beautiful to observe, but without it all life upon the earth would shortly have to cease. To speak of microbes as if they were all malignant is wholly erroneous. Every living thing must die sooner or later; yet, as we know, though life has flourished upon the earth for untold ages, and though living creatures have died in unthinkable millions throughout every year of those ages, the earth is not covered mountain high with corpses. All dead bodies, animal or vegetable, high or low, terrestrial or marine, are resolved by microbes into simple elements which are thereby set free for the service of the generations to come. The bacteria of putrefaction suggest nothing wonderful, least of all do they suggest life. Yet at any moment these germs of death are necessary links in the chain which leads to future life. Thus the ferments by which these microbes do their work must earn our recognition. Without their powers mankind could never have been produced at all. To-day, as throughout the ages, they continue the work of putrefaction, which to the superficial eye is nothing but hideousness and horror, but to the seeing eye has in it the promise of all the life that is to be. Every living creature must die and return to the dust. There its body is resolved by fermentation into the simple substances which we often call manure. The wisest of the poets have seen the beauty and the wonder of this process, as in Tennyson's couplet:

“And from his ashes may be made
The violet of his native land,”

and Hamlet's:

“And from her fair and unpolluted flesh may violets spring.”

Thus, if the fermentations which result in life cannot avert inevitable death, yet all death in virtue of fermentation makes for future life. You may be selfish for a century, but at the last others will claim your dust, and we are linked throughout the ages, “Buried, and breathing and to be,” as George Meredith has said.

Lastly, I believe that in the complete solution of the problems of fermentation will be found the revelation not only of the physical nature of life, but of its origin upon the earth. Robert Louis Stevenson saw deeply when he said that even mankind is in a sense the “vital putrefaction of the dust.”

We must be fair, then, in our reckoning with the ferments. They hold the keys both of life and death. The ferment of the yeast plant, with its product alcohol, has cursed our kind for ages, and curses it to-day. All the diseases of which we die may be expressed in terms of morbid fermentation; but on the other hand, life itself, physically considered, is a series of fermentations. Even when it is threatened by disease, such as cancer, the introduction of a new series of fermentations may avert death; and without the ferments by means of which the microbes of putrefaction do their work, the whole history of life upon the earth would have been no more than the history of a rocket, full of apparent promise, but doomed to instantaneous destruction.

CHAPTER X

THE CHEMISTRY OF CANCER

LOUIS PASTEUR, one of the supreme interpreters of Nature of all time, was "a mere chemist," and "not even a medical man." Nevertheless, he was one of the makers of modern biology and the father of preventive medicine. Before we consider the relation of his work, as Dr. Beard sees it, to our present subject, it will be not inappropriate, in the light of recent events, to quote certain words of his which may be commended to the general consideration to-day: "What," he said, "I have been engaged for twenty years in research on a subject, and have no right to an opinion! And the right of verifying, controlling, discussing and questioning belongs more especially to him who has done nothing to clear up the matter, to one who has just read my works more or less attentively, with his feet on the mantelpiece!"

Pasteur's first original piece of work, and that which led him astray, as his great teachers Dumas and Biot thought, from chemistry (so that he ultimately created the science of bacteriology), was the discovery that certain living organisms will digest or ferment certain molecules of tartaric acid, while leaving untouched other molecules identical in all respects except that they differ as a right hand differs from a left. The key fits the lock, the hand the glove; but the right hand will not fit a left-handed glove.

Since the one set of crystals rotates the plane of a ray of polarized light to the right, and the other rotates

it to the left, the first are called dextro-rotatory, and the second lævo-rotatory. The yeast ferment acts upon the lævo-tartrate only; the ferment of the mold, *Penicillium*, acts upon the dextro-tartrate only.

The two sets of crystals are called isomeric or isomers; and the fact is noteworthy that when any of these isomeric compounds are manufactured in the laboratory, the result appears to be neutral to the ray of polarized light. This is due not to the creation of a neutral isomer, but to the fact that the product is really a mixture in equal proportions of the dextro and the lævo compounds. Pasteur noted, indeed, that all the artificial products of the laboratory, unlike all naturally occurring organic compounds, are without action on polarized light: they consist of equal proportions of oppositely-acting compounds; but they can be separated from each other by the action of specific ferments. In the words of Duclaux, Pasteur's successor, "Nature alone knows how to manufacture the one isomer without producing the other. A living cell is a laboratory of dissymmetrical forces, or a dissymmetrical protoplasm, acting under the influence of the sun."

"I have, in fact," said Pasteur in 1860, "set up a theory of molecular asymmetry, one of the most important and wholly surprising chapters of science, which opens up a new, distant, but definite horizon for physiology."

This great doctrine is now recognized to depend upon the fact of the "asymmetry of the carbon atom," first stated by Van't Hoff and Le Bel. It is, indeed, a chief tenet of the new science of stereo-chemistry, or the chemistry of three-dimensioned space, which conceives of molecules as "solid" things, extended in the three dimensions of space. Since the carbon atom is asym-

metrical—and also the five-handed or pentavalent nitrogen atom, as Wislicenus declared in 1877—isomeric compounds in general may be built up in two directions, so that the one compound is the mirror-image of the other. The classical instance is the carbon compound called tartaric acid, as investigated by Pasteur. We shall now see that, according to Dr. Beard, this initial discovery of Pasteur actually constituted the foundation of the science of ferments, *with all that depends upon it*.

Pasteur's work began with this discovery of an antithesis; and Dr. Beard's work, as we know, began with the discovery of an antithesis between structures peculiar to alternate generations in the life-cycle of a fish. It is now his contention that the "antithetic alternation of generations," as he calls it, ultimately depends upon the same fact as the antithesis discovered by Pasteur, viz. the asymmetry of the carbon atom. That "laboratory of dissymmetrical forces," which we call the cell, builds up certain molecules in one generation and their mirror-images in the next.

Dr. Beard quotes the observation of Mellor, "that only the dextro-sugars occur in nature, and that these are the only sugars which can be assimilated as foodstuffs by the yeast plant." Hence, according to Pope (*Nature*, vol. 68, p. 280, 1903): "It would seem to follow, as a legitimate conclusion, that while dextro-glucose is a valuable foodstuff, we should be incapable of digesting . . . lævo-glucose. Humanity is therefore composed of dextro-men and dextro-women. And just as we ourselves would probably starve if provided with food enantiomorphously¹ related to that to which we are accustomed,

¹Enantiomorphism was Pasteur's name for the relation between a compound and its mirror-image.

so, if . . . lævo-men were to come among us now . . . we should be unable to provide them with the food necessary to keep them alive." Pasteur himself remarks: "Perhaps this will disclose a new world to us. Who can foresee the organization that living matter would assume, if cellulose were lævo-rotatory, instead of being dextro-rotatory, or if the lævo-rotatory albumins of the blood were to be replaced by dextro-rotatory bodies?"

Says Dr. Beard: "In the light of the antithetic alternation of generations and of the natural antithesis of the compounds arising in the two generations, the following passage from p. 283 of Professor Pope's address is of interest. It is also instructive in view of the generally accepted, but false, views of the question. 'Again, suppose that at its origin life were carried on non-enantiomorphously, and that it involved the consumption and the production only of non-enantiomorphous substances and of compensated mixtures, it may well be foreseen that a stage in development might arise when each individual, in view of the increasing complexity of his vital processes, would have to decide to use only the one enantiomorphous component of his compensated food, and so evade an otherwise necessary duplication of his digestive apparatus. Acting intelligently or fortuitously, one-half of the individuals would become dextro-beings, while the other half would become lævo-individuals; the succeeding generations would thus be of two enantiomorphously related configurations.' He then goes on to express his own opinion, that in course of time one configuration, the weaker one, would permanently disappear. But in this opinion the facts of botanical and embryological science are not taken into account. It is only, however, necessary to make the 'succeeding generations'

spoken of alternate, in order to meet the scientific requirements of Nature, and so to make the passage absolutely true as a statement of scientific fact. This is done by inserting in the closing passage the word 'alternating,' when it would read: 'The succeeding generations alternating would thus be of two enantiomorphously related configurations.' "

Dr. Beard notes how, in these two last quotations, we may find at least a hint of the conceivable existence of an antithetic generation in which the chemical compounds are enantiomorphously related to those in our own bodies. In order to exist, the "lævo-men" of Pope "would need to be able, by means of ferments, to pull down all our food-substances, and to rebuild in the opposite, or enantiomorphously related, or antithetic direction." "But," says Dr. Beard, "these hypothetical 'lævo-men' do exist among us, and they do pull down and build up again in the opposite direction, *for the 'lævo-men' are the cancers.*"

As a recent quotation has shown, Pasteur himself, with his supreme insight, did foresee that his theory of molecular asymmetry opened up a new horizon for physiology: that in it, indeed, as Dr. Beard now avers, is the basis of a science of comparative physiology. Pasteur was not a biologist by training, and he was not acquainted with the researches of Hofmeister and others, already published, on the life-cycle of various plants and their alternation of generations.

"Now," says Dr. Beard, "if there be a dextro-cellulose, or a lævo-albumin, or a dextro-sugar, or a dextro-glycogen, stereo-chemistry asserts the possibility or the necessity of the occurrence of a lævo-cellulose, a dextro-albumin, a lævo-sugar, or a lævo-glycogen. This the reader

will find laid down on p. 14 of Meyerhoffer's translation of Van't Hoff's work. As Duclaux quite rightly perceives, to obtain the change from the one direction of asymmetry to the other, it is necessary to go back to the 'germ.' Like the cellulose of a flowering-plant, a rose or an oak tree, that of the fern-plant is dextro-cellulose. But in the life-cycle of the fern, as in that of the flowering plant, there are two generations, the asexual one, or fern-plant, and the sexual one, the small and insignificant prothallus. As the cellulose of the fern is dextro-cellulose, so that of the prothallus must be lævo-cellulose, and so with the other naturally occurring organic compounds. None such found naturally in an asexual generation of a plant, or in a sexual generation of an animal, will be met with in the corresponding sexual generation of a plant or asexual generation of an animal; but, if occurring at all, it will be represented by a compound with the opposite rotation."

Elsewhere I discuss the specific action of ferments, fitting the substance upon which they act as a key fits a lock, or a right hand a right-hand glove, but not a left-hand glove of the same size and make. The ferments must be conceived in terms of stereo-chemistry as "solid" structures, capable of interlocking with, and acting only upon, substances of "opposite isomeric form."

Now the cancer-ferment, "malignin," as we know, acts upon and pulls down the lævo-albumins of the living human body. *Per contra*, trypsin, as has been repeatedly proved by Von Leyden, Blumenthal, Bergell, Pinkuss, Neuberg and Ascher in Germany alone, has a similar specific action upon the albumins of cancer. Dr. Beard, therefore, suggests that the specific albumins of cancer—the existence of which has been demonstrated beyond

all doubt by the German observers—must be dextro-rotatory. “As the lævo-albumins of the living human body are not acted upon by trypsin, whereas the albumins of a living cancer are, it follows . . . that the latter must be dextro-albumins.”

Take now the action of amylopsin. This ferment readily converts the dextro-glycogen of the liver, but has no action upon the glycogen proper to cancer, which must therefore be a lævo-glycogen.² The use of amylopsin in cancer is not to digest its glycogen at all.

Says Dr. Beard: “Just as isomeric compounds in the form of starches occur in both generations of plants, so also isomeric compounds of glycogen or animal starch are found in sexual and asexual generations of animals, including cancer. But if the dextro-compound occurs naturally in the one generation, the lævo- one will obtain in the other. Mellor remarks that only the dextro-sugars or glucoses are known to occur naturally. This is because the chemical composition of the sexual generation of any plant—a fern-prothallus, for example—has never yet been determined in the laboratory. It is not true of animal life, for as long ago as 1859, forty-eight years ago, Claude Bernard found lævulose, or lævo-sugar, in the allantois. According to him, it disappears towards the fifth or sixth month of intra-uterine life of the calf, a fact that goes to show this lævo-sugar to be formed in the trophoblast, and not in the allantois. Doubtless, its disappearance coincides with the development of large numbers of leucocytes in the fœtus. To my knowledge, this lævo-sugar has more recently been rediscovered in

²The fœtal pancreas produces no amylopsin. Even a child six months old cannot digest starch, since no amylopsin is produced by the pancreas until after the first year.

the placenta, but I am not aware that the fact has been republished. Of course, the allantois and the placenta are synonymous, but the real source of the lævulose in both instances was the asexual generation or trophoblast."³

The antithetic alternation of generations, then, depends upon the asymmetry of the carbon atom, the existence of isomers, and the specific and antithetic action of the ferments which can act upon them.

"With the start of the sexual or the asexual phase of the cycle the naturally occurring compounds are built up in the one direction or in the other. With the beginning of the next phase of the cycle—the alternate one, sexual or asexual—the swing of the pendulum about the asymmetrical carbon atom is on the other side, and the naturally occurring organic compounds are built up in the opposite direction. In animal life, that of the higher animals, the compounds are built up after the fertilization of the egg and in the life-period of the asexual generation in the direction of lævo-sugar, lævo-glycogen and dextro-albumins. This evolution of compounds is the antithesis of that which obtains with the unfolding of the sexual generation, the embryo or individual. Here the naturally occurring organic compounds are evolved in the direction of dextro-sugars, dextro-glycogen and lævo-albumins."

Animals and plants are to be compared in this respect. The sexual generation of animals is characterized by dextro-sugars, dextro-glycogen and lævo-albumins. In the corresponding sexual generation of plants, such as

³It may conceivably be relevant, I think, to observe that the breast, a very common site of cancer, normally produces lævulose, a lævo-sugar.

the fern-prothallus, these are absent, being replaced by their oppositely-rotating isomers. Thus it is the *asexual* generation of plants (the flowering-plant) and not the sexual generation, as in animals, which possesses dextro-sugar, dextro-starch and dextro-albumins. Observe the planetary significance of this.

As we saw in the last chapter, all animals depend for their food upon plants. Says Dr. Beard: "Were the sexual generations of plants the produce of the foodstuffs of animals, the latter, owing to the insignificance of the former, would find existence a very serious problem. The sexual generations of plants form substances resembling those fabricated by the asexual generations of animals, trophoblast or cancer. Even if obtainable in sufficiently large quantities, the substances found naturally in a cancer would not be suitable as the foodstuffs of an animal—a man, for example. But as the asexual mode of reproduction, whether of a plant or of a cancer, is the most prolific one, there has hitherto, at all events, been no failure on the part of the asexual generations of plants to furnish ultimately the foodstuffs of the animals. The conditions met with in animals are reversed in plants. Here a lævo-cellulose, a lævo-sugar, a lævo-starch, and one or more dextro-albumins must be sought for, not in the asexual generation as in animals, but in the sexual one, as represented by, for example, the fern-prothallus."

The matter may be stated in the following table (Beard):—

ANIMAL

Sexual Generation or Individual.

Lævo-albumins, not acted upon when living by trypsin, but attacked in life and pulled down by the cancer-ferment, malignin.

Dextro-sugars.
Dextro-glycogen.
Pigment melanin.

Asexual Generation (trophoblast or cancer).

Dextro-albumins, not acted upon when living by their own intra-cellular ferment, malignin, but attacked in life by trypsin.
Lævo-sugar.
Lævo-glycogen.
Pigment, not melanin (in melano-sarcoma, Blumenthal).

PLANT

Asexual Generation (flowering-plant or fern).

Lævo-albumins.
Dextro-starch.
Dextro-sugars.

Sexual Generation (fern-prothallus).

Dextro-albumins.
Lævo-starch.
Lævo-sugars.

One more quotation from Dr. Beard is necessary:—

“In 1889, in his study of the placentation of the hedgehog (*Erinaceus europæus*), Prof. A. A. W. Hubrecht set up the term trophoblast, at the same time assigning to it, as the name implies, a nutritive significance. The nutritive import of the trophoblast of normal mammalian gestation has since that time been confirmed by many other embryologists, notably by E. van Beneden and M. Duval, and it has been ‘generally accepted.’ In the light of our present knowledge a significance different from that seen in it by Professor Hubrecht must be recognized in ‘trophoblast.’ Trophoblast has, and can have, no nutritive import for the developing embryo. This is quite obvious, once it is noted that the natural compounds formed in it are built up in the wrong direction to be

useful as food for the developing sexual organism. The term, therefore, cannot be employed in future in a physiological sense. As Duclaux said, 'Nature alone knows how to manufacture the one isomer without producing the other.' The chemist in the laboratory manufactures equal amounts of both isomers. May one deny nature the power to do the like on occasion? Certainly not. It must be concluded, that in the fertilized egg she can build up in both directions. By the first few cleavages of the egg, usually the first three to five, she can separate off portions as cells, endowed solely with the powers of producing the isomeric compounds of trophoblast, whilst retaining for the cell in the line of heredity the property of forming both. With the start of the evolution of an embryonic body, again by cell-division, she can separate off one or more original embryonic cells with powers opposite to those possessed by trophoblast, all this taking place before any extra-cellular enzymes, such as trypsin and amylopsin, are formed. Full agreement, therefore (in a sense), may be expressed with the conclusion of Duclaux, that 'to introduce in a cell principles immediately different and the inverse of those which existed there, it is necessary to act upon it at the moment when it is most plastic, to take the cell of the germ and try to modify it' (p. 66). But as Duclaux also observes, this cell has a heredity, and these determine not only its being, but what it shall become."

I believe the reader will agree with me that the beauty of this final theory of Dr. Beard's rivals that which led him to indicate trypsin as the naturally appointed remedy for cancer. But it is not therefore necessarily true, and it is here submitted as a hypothesis for consideration, not for acceptance. We must remember that, as Goethe

said, "Hypotheses are the cradle songs with which the teacher lulls his pupils to sleep."

Some less general aspects of the chemistry of cancer will be considered in the chapter which deals with the German work upon this subject, but here I reprint for the student the list of Dr. Beard's references appended to the paper of which this chapter is a summary.

LITERATURE CITED IN REFERENCE TO THE PRECEDING CHAPTER

- BEARD, J. The Early Development of *Lepidosteus osseus*, in *Proc. Roy. Soc. Lond.*, vol. 46, pp. 108-118: 1889.
- The History of a Transient Nervous Apparatus in Certain Ichthyopsida: An Account of the Development and Degeneration of Ganglion-Cells and Nerve-Fibres: Part I., Raja batis, in *Zool. Jahrb., Morph. Abteil.*, vol. 8, pp. 1-106, 8 plates: 1896.
- On Certain Problems of Vertebrate Embryology (The Critical Period, etc.), pp. 1-77: Jena, Gustav Fischer, 1896.
- The Span of Gestation and the Cause of Birth, pp. vi and 132: Jena, Gustav Fischer, 1897.
- Embryological Aspects and Etiology of Carcinoma, in the *Lancet*, June 15, 1902.
- A Morphological Continuity of Germ-Cells as the basis of Heredity and Variation, in *Rev. Neur. Psych.*, 1904.
- The Cancer-Problem, in the *Lancet*, Feb. 4, 1905.
- The Interlude of Cancer, in *Medical Record*, Feb. 2, 1907: New York.
- The Scientific Criterion of a Malignant Tumor, in *Medical Record*, Jan. 5, 1907: New York.
- BERGELL, P. Zur Chemie der Krebsgeschwülste, in *Zeitschr. f. Krebsforschung*, vol. 5, pp. 204-208: 1907.
- BERNARD, CLAUDE. Lecons de Physiologie expérimentale, vol. 1: 1853, Paris.

- BLUMENTHAL, F. Die chemische Abartung der Zellen beim Krebs., in *Zeitschr. f. Krebsforschung*, vol. 5, pp. 182-189: 1907.
 Die chemische Vorgänge bei der Krebskrankheit, in *Ergebn. d. Exper. Path. u. Therap.*, vol. 1, pp. 65-104: 1907.
- CLEAVES, M. A. The Physiological Action of the Pancreatic Enzymes, with special reference to Hematology, Urinology, and Clinical Pathology, in *Medical Record*, June 1, 1907: New York.
- CORVISART, LUCIEN. Sur une Fonction peu connue du Pancreas, pp. 1-123: Paris, 1857-8.
- DUCLAUX, E. Pasteur: Histoire d'un Esprit, pp. i-vii and 1-393: Paris, 1896.
- HOFMEISTER, WILHELM. Vergleichende Untersuchungen: 1851.
- HUBRECHT, A. A. W. The Placentation of *Erinaceus europæus*, in *Quart. Jour. Micros. Sci.*, vol. 30, pp. 283-404, 13 plates: 1889.
- KÜHNE, WILHELM. Ueber das Verhalten verschiedener organisirter und sog. ungeformter Fermente, and Ueber das Trypsin (Enzym des Pankreas), in *Verhandl. des Heidelb. Naturhist. Med. Vereins.*, N.S. I. 3, pp. 1-10: 1876.
- LEYDEN, E. VON, u. BERGELL, P. Ueber die therapeutische Anwendung von Pancreatin in Carcinoma, in *Zeitschr. f. klin. Med.*, vol. 61, pp. 360-365: 1907.
- MELLOR, J. W. Chemical Statics and Dynamics: London, 1904.
- PASTEUR, LOUIS. De la dissymétrie moléculaire des produits organiques naturels. *Leçon professée devant la Société chimique*, 1860.
- POPE, WILLIAM J. Recent Advances in Stereo-Chemistry, in *Nature*, vol. 68, pp. 280-283: 1903.
- RICE, CLARENCE C. Treatment of Cancer of the Larynx by subcutaneous injection of Pancreatic Extract (Trypsin), in *Medical Record*, Nov. 24, 1906, pp. 812-816: 1906, New York.
- SACHS, JULIUS VON. Geschichte der Botanik: Munchen, 1875.

- WIGGIN, F. H. Case of Multiple Fibrosarcoma of the Tongue, in *Jour. Amer. Med. Assoc.*, Dec. 15, 1906, pp. 2003-2008.
- RICHARDSON, G. M. The Foundations of Stereo-Chemistry, Memoirs by Pasteur, Van't Hoff, Lebel, nx. Wislicenus. Translated and edited: New York, 1901.
- HOFF, J. H. Stereo-chemie. Nach Van't Hoff's Dix années dans l'histoire d'une theorie neu bearbeitet von W. Meyerhoffer: 1892.
- WEDEKIND, EDGAR. Zur Stereo-chemie des fünfwertigen Stickstoffes: Leipzig, 1899.
- VALLERY-RADOT, RENÉ. La Vie de Pasteur: Paris, 1901.

PART II—PRACTICAL

CHAPTER XI

CANCER AND SURGERY

UNTIL the recent inquiries which this book discusses, it was generally recognized that, despite all other promises, there was no means of opposing the growth of cancer but the knife. The local treatment, whether by the knife or caustics, of what is at first a local disease in every case, dates back to the earliest times. At one period during the nineteenth century the view was strongly expressed, and held, that though the manifestations of malignant disease are primarily local, the malady really has its seat in the blood, and that therefore all local treatment is essentially futile. Now it may very probably be true that certain conditions of the blood are highly relevant to the growth of cancer, but no one would as yet again oppose the surgical treatment of cancer on the grounds which were formerly maintained. For many years past, and, indeed, ever since the immortal work of Lister made possible the scientific development of surgery, such advance as has been achieved in the treatment of cancer has been entirely surgical. The solitary exception, perhaps, is that of the treatment by the Röntgen rays of the most superficial and least malignant form of cancer, which is known as rodent ulcer. The surgeons and the pathologists have joined hands to ascertain, in the case of cancer occurring in various sites, the directions in which the disease commonly spreads, and the position of the

lymphatic glands in which secondary growths commonly occur. These investigations have led to the devising and making of ever more and more extensive operations. Not so very long ago, for instance, the surgeon was content merely to excise visible cancer of the tongue or lip; now, in addition to doing so, he systematically removes all the neighboring lymphatic glands, whether they be obviously enlarged or not. Similarly, time was when, for cancer of the breast, that organ alone was removed, but for some few years past no surgeon would be regarded as competent or conscientious who did not completely clear out all the lymphatic glands in the arm-pit and above the collar-bone of the affected side. In later years much more radical operations for cancer of the breast have been carried out, even to the extent of removing a great deal of the muscular tissue underneath the organ.

The surgeons, however, have had to fight against difficulties perhaps more serious even than those inherent in the nature of the disease itself. These difficulties may be summed up as fear and ignorance on the part of the patient, and ignorance on the part of the doctor. This latter difficulty has been very largely disposed of in later years. Enormous improvement has taken place in the early diagnosis of cancer, as well as in its diagnosis at all stages, and it is this increased recognition of the disease that probably accounts for the apparent increase in its occurrence. I am not acquainted with any conclusive evidence which shows that the incidence of the disease is actually increasing. When this difficulty is removed, however, there remains the fear and the ignorance of the patient, and lately efforts have been made in Germany and in this country to combat this state of things. The German efforts mainly took the form of a newspaper crusade,

designed to warn women of the necessity for inquiring closely into certain symptoms occurring at certain ages, which they too often disregard. The hope was that thus many early cases would come up for treatment when the surgeon might reasonably hope for substantial results from his interference; and this expectation has apparently been justified in some measure.

Now, though this volume constitutes, as I believe, a most serious portent for the surgeons from the financial point of view, it is well to have it clearly understood that the writer has no bias whatever against surgery or surgeons, or the surgical treatment of cancer. On the contrary, until these new discoveries, I was most firmly convinced of the importance of surgery as the only hope for the victim of cancer, and fortunately I can prove that it was my desire to aid the surgeons as far as might be in their struggle against this disease. In addition, therefore, to many published statements of mine on this point, I asked a distinguished English surgeon to contribute to *The New Library of Medicine*, of which I am the editor, a volume which should discuss the duty of the public to itself in respect of the recognition of cancer at stages which the surgeon may hope to control. I shall here avail myself of certain facts cited in that volume¹—facts which retain their importance despite all present or subsequent developments in the non-surgical treatment of cancer. We must remind ourselves that the importance of early treatment, in any case, can scarcely be overestimated. *Nothing could be more disastrous than the creation of a belief that it does*

¹*The Control of a Scourge; or, How Cancer is Curable.* By C. P. Childe, B.A., F.R.C.S. *The New Library of Medicine*: Messrs. Methuen & Co.

not now matter at what stage cancer is treated—the belief that the ferments can be trusted at any stage, or that it does not matter when the knife is employed now that it has the ferments to help it. We have to remember that, just as tuberculosis destroys lung-tissue, which no conceivable treatment can re-create, just as the most trivial cut in the skin, though it heals in a couple of days, involves the permanent destruction of cutaneous structures, so the growth of malignant tissue involves a destruction of healthy tissues, which no treatment, though it were instantaneous and absolute, can conceivably restore. Assuredly, it remains of the greatest importance that cancer be recognized early, but on account of the damage which it causes, the pain involved in its growth, and the length of time which will be necessary for treatment.

The great surgeon, Sir Benjamin Brodie, after operating on not far short of six hundred cases of cancer of the breast, "came to the conclusion that life was rather shortened than prolonged by his efforts in this direction, and decided never to remove another breast for cancer without first laying before the patient his experience of its results." In his lectures on Surgical Pathology, Sir James Paget said: "I will not say such a thing as cure is impossible, but it is so highly improbable that a hope of this occurring in any single instance cannot be reasonably entertained." The results of recent surgery, however, are very different, and if we accept what is called the three years' limit we shall find that many cures may now be obtained. This three years' limit is, of course, an entirely arbitrary one, and it is certainly not possible to say that a cancer, if it is to recur at all, always recurs within that limit; but the figure is of some practical

utility.² We may note in passing the absurdity of the argument which has been advanced against some of the reported cures by the pancreatic treatment, that no mention should be made of any results until three years have expired: as if this three years' limit were a law of nature. It almost beggars belief that any one should apply the same criterion to the disappearance of an active tumor under hypodermic injections, as to excision by the knife. The reader may be referred to Mr. Childe for recent statistics which show that adequate operation in early cancer sometimes effects real cures. I, for one, have no desire to underrate this fact, nor to deny great credit to the surgeons for their efforts.

The chief difficulty of the surgeons I have asserted to be the lateness of most operations. Mr. Childe very clearly shows how women, aware of a lump in the breast, will delay for periods—sometimes of months, sometimes as many as two, three or five years—before they seek advice. On the other hand, when the surgeon has a fair chance, he may undoubtedly succeed in effecting true cures of cancer. One distinguished surgeon, for instance, quoted by Mr. Childe, says, "I am strongly of opinion that lip cancer seldom returns if operated on thoroughly and sufficiently early." All the surgical authorities are agreed that "the elimination of this disastrous factor, delay," would make an enormous difference in the surgical treatment of cancer.

In the endeavor to present an absolutely impartial statement of the facts, however, we have to recognize another side of this question. Believing, as we must, that the cancerous tissue is of a specific kind, and has a specific

²It has recently been shown that the disease recurs in at least one-fourth of those who are called cured at the end of three years.

origin, we need not question that if the surgeon succeeds in removing the whole of it, there will be no recurrence of the disease. We may also incline strongly to the view that the explanation of recurrence, when it occurs, is to be sought in the inadequacy of the removal. Surgeons have often asked whether this was the explanation or whether the disease simply made a fresh start in the neighborhood. All the surgical evidence goes to show that this last is not the explanation, and Dr. Beard's theory of the nature of cancer points in the same direction. On that theory a recurrence after complete removal would not be, properly speaking, a recurrence at all, but the malignant development of a new germ-cell which happened to be in the neighborhood, and which found conditions favorable to its multiplication. Such a coincidence would be extremely improbable. But we have to reckon with the fact that in the vast majority of cases the surgeon does not remove the whole of the malignant tissue. He removes part, very likely the greater part, but he leaves some of it, and that, by his interference, he may possibly affect. His knife cuts through it. It is very possibly exposed to the action of antiseptics, and in some cases, doubtless, these may be so powerful as actually to kill a certain number of cancer-cells together with the normal cells of the tissues surrounding them. But what will be the effect of these injurious influences upon the cancer-cells which are neither removed nor killed?

In seeking to answer this question we must reckon in the first place, with a large number of clinical facts, and for certain of these I am indebted to a recent volume³ by Dr. John Shaw, himself formerly a distinguished

³*The Cure of Cancer, and How Surgery Blocks the Way.* By John Shaw, M.D. (London). F. S. Turney. 1907.

surgical operator. There is much evidence to show that when cancer recurs after operation, it is apt to grow more rapidly and to show more malignancy than before. In recent years, the increment of mortality from cancer has been enormous, notwithstanding the very great extension of surgical activity against this disease. Now, Sir James Paget, a generation ago, in his famous lectures on Surgical Pathology, comments upon cases in which a tumor, apparently innocent, is removed, but some time after a cancer appears at the same part. He suggests that "in the removal of this tumor, the surgeon has unwittingly supplied by the local injury what was needed for the production of a cancerous growth: he has made some locality apt for the manifestation of a constitutional disease already existing." Now, without unreservedly accepting the definition of cancer as a constitutional disease, we may note the suggestion by this great man, whose pathological insight amounted to absolute genius, that the local injury involved in operation may, in effect, constitute a stimulus towards the development of cancer. Elsewhere in the same famous volume Paget says: "A tumor which at first might be not unlike the normal fibrous or glandular texture in which it grew, after repeated removal and recurrences becomes softer, more succulent, and in its later growths may seem to the naked eye little more than like masses of yellow or ruddy soft gelatine with blood-vessels. The latter are usually much more rapid in their progress than the earlier growths, they are generally less well defined, penetrating farther and more vaguely among the interstices of adjacent parts, and more quickly protruding through the skin or scars over them. And in these characters the later-formed tumors assume more of the character of malignancy than the earlier. . . . In

one of Prof. Gluge's cases the transitions to completely malignant characters appeared yet more sure. Mr. Syme also expresses a similar transition; describing as the usual course of the cases he has seen, that, after one or two recurrences of the tumor, the next new productions present a new degeneration of character, excite pain, proceed to fungous ulceration, and thus in the end prove fatal. So that, although there be cases in which this evil career has not been run, yet I think we may regard these tumors as approximating to characters of malignancy, not only in their proneness to recurrence after removal, but in their aptness to assume more malignant features the more often they recur. Whatever be the truth concerning the supposed transformation of an innocent into a malignant morbid growth, I think it can hardly be doubted that, in the cases of some recurring tumors, the successively later growths acquire more and more of the characters of thoroughly malignant disease." Note also the statement of Prof. Godlee regarding a certain kind of malignant tumor that "Sarcomata present all degrees of malignancy; but, as a rough rule, it may be stated that the higher the degree of development of the tumor, the less likely is recurrence to take place after removal. In connection with this point, it is interesting to note that each recurrence of a sarcoma often shows a more rudimentary structure, and, at the same time, a greater degree of malignancy."

Closely allied, as we may see, to the facts above quoted, are certain consequences which may sometimes follow the practice of removing a small portion of a tumor for purposes of microscopical examination. In such cases it has sometimes happened that the tumor, after the performance of what is practically a very inadequate opera-

tion for removal, shows rapid growth. Dr. Shaw's conclusion from the evidence which he adduces runs thus: "On the evidence already presented, I submit that the conclusion is incontrovertible, that operation may induce malignancy in structures which beforehand were devoid of all such characteristics." The experimental evidence regarding the behavior of cancer in mice strongly confirms this opinion, and though I cannot assent to Dr. Shaw's explanation of the facts, I believe that the facts are established. Every one recognizes, the surgeons included, that irritation may excite cancerous growth, and in the case of warts upon the face, for instance, the surgeon always discourages the application of caustics for fear of this consequence. But it is evident when we come to consider the matter that the performance of an imperfect operation for cancer involves the application of very serious irritation to the living cancer-cells which are not removed, and the irritation which will arouse a cancerous growth from its germ may reasonably be expected to increase the vitality of a growth already present. I am not aware that any surgeon has made this obvious observation.

If now we turn to the *Zeitschrift für klinische Medizin*, vol. 61, pp. 360-365, 1907, we find the greatest official authority upon cancer in the whole world, Prof. Ernst Von Leyden, laying down a great principle regarding the growth of cancer. It is that malignant tissue in general is characterized by the response of increased growth in consequence of all forms of injury, whether mechanical, chemical or thermal. This is not to say, of course, that injury will not kill malignant cells, but that the cells which are not killed (or removed, as by the knife) will tend to grow not less but more in consequence

of the injury. In short, they respond to the irritation of the injury, just as the cells of a pigmented mole may respond to the application of caustics. This principle, subscribed to by Von Leyden, is in entire accordance with the clinical facts which we have lately been considering. It constitutes a general expression of such facts as the accelerated growth of a recurrent tumor and the more malignant type which such a tumor displays, both as regards its behavior and as regards its microscopic structure. Here I may note—though it is not our immediate concern—that after his work with trypsin, Von Leyden declares himself to have recognized a new fact. He found that trypsin acted as an injurious agent upon cancerous tissue in the body, as was proved by its actual dissolution of such malignant cells as were exposed to it. But he never found that this injurious action was subsequently responded to by increased growth, either locally or generally, on the part of the remaining cells. This, as Von Leyden recognizes, is a new and a unique fact, constituting the only exception to the principle of increased growth after injury which has already been laid down.

This principle of increased growth and malignancy has to be reckoned with by the surgeon, and it is of interest to observe that its operation may be recognized, even in the case of the one other influence which, besides trypsin, seems to have a specific injurious action upon malignant cells. This is the case of the Röntgen rays, and of radium, acting, as I surmise, by means of its *gamma* radiation, which is essentially the same as the Röntgen rays. Here there would seem to be a specific action upon malignant tissue, but in the overwhelming majority of cases where this action does not amount to

the complete destruction of all the offending cells, the principle of increased growth after injury may be manifested. Unfortunately also there is evidence that the Röntgen rays may actually excite malignant growth *de nova* in certain cases. Trypsin, therefore, and possibly other ferments, are alone in their relation to this principle.

How, then, do these facts bear upon surgical practice at the present day, so far as malignant disease is concerned?

In the first place, I do not make any suggestion or proposal that *complete* surgical operation, when practicable, should not be employed for cancer. Though inadequate operations certainly stimulate the growth in accordance with the law laid down by Prof. Von Leyden, we now have means which *may* neutralize that stimulation, while operations on early cases, removing the whole disease, are often now-a-days completely successful. I believe the time will come when the knife may be discarded for the cancrotoxic ferments, but it has not yet come. I desire nothing less than to dissuade patients at this stage from availing themselves of all the real help that the surgeon can give them. It may be clearly recognized that in early and suitable cases modern surgery may remove the whole disease finally without any appreciable risk, and with a rapidity which no other mode of treatment can emulate. Furthermore, there are other cases of advanced internal cancer in which surgery can perform what are called plastic operations, that go some way towards compensating for damage which has already been done by the disease, and which no conceivable treatment can make good. In the present state of things, then, the surgeon's help is by no means to be dispensed with.

But no matter how early the case or how radical the operation, trypsin and amylopsin, or more effective ferments, if such exist, should also be employed from the first, and no less vigorously after the operation than before it, in order to avert the recurrence which follows the overwhelming majority of even the most extensive operations. I honor the surgeon, unknown to me, who wrote a column-long letter, signed "F. R. C. S.," to the *Morning Post* (April 16, 1907), extolling the use of trypsin in cancer, for his public advocacy of a mode of treatment which may prove to be the most serious matter financially to the surgical profession; but meanwhile the surgeons also may benefit as regards reputation and results, if they will use these remedies in addition to the knife. It cannot possibly be doubted that a successful non-surgical method of treating malignant disease must constitute a serious menace to the pockets of operating surgeons. This obvious assertion has been questioned. It has been truly said "the profession can only gain by any increase of its resources against disease," and that is certainly true in the great sense; but the fact certainly remains, that if operations for cancer were to become unknown, the surgeons would find a very large part of their occupation gone. The utmost honor is therefore due to the one or two surgeons who have seriously looked into the new principle of treatment, and it is earnestly to be hoped that they may have their reward. At the time of writing I know of one such in America, the writer of the *Morning Post* letter, and one other in Great Britain, and Prof. Bier in Germany.

On further consideration I see, however, that it will not do to leave the question thus. As Dr. Hale White

pointed out in the "Address in Medicine" delivered before the British Medical Association at Exeter, in August, 1907, it is a source of the gravest error to act in practice upon the results obtained by the most skilful surgeons. Take the common instances of cancer of the breast or tongue. The surgeons throughout the world at the present day who perform really adequate operations in such cases, even when they are taken in time, certainly do not run into three figures. Only one patient in many thousands is fortunate enough to come under their hands. The adequate operation for cancer is the excessively rare exception. It is right that the results thus obtained should be published and the obvious argument drawn from them, as is done by Mr. Childe, but it is grossly fallacious to assume that these results might and would be attained everywhere if patients would come up for operation in time. To the *British Medical Journal* (July 20, 1907) Mr. Childe himself contributed an article, entitled "The Educational Aspect of the Cancer Question," which abundantly demonstrates the need for educating not only the public but also the generality of surgeons. He lays down the proposition, which will be generally accepted, that "every recurrence is owing to omission on the part of the surgeon to overtake the centrifugally spreading disease." Now recurrence is the all but invariable rule, if the whole of surgery for cancer be reviewed, and not merely the work of, say, two surgeons in one capital and one in another. Furthermore, even the most accomplished surgeons have a large percentage of failures, despite the fact that the modern radical operations have now reached something like the utmost limit of the practicable. Now it is necessary, plainly, not to write as if every surgeon were a past-

master and as if every patient applied for treatment at the earliest possible stage. These conditions are highly desirable, but they are not actual, and the actual is our concern here.

In the light of the clinical facts above recorded as to the increased malignancy of growths recurrent after operation, and the law laid down by Von Leyden, it is necessary to question very gravely the assumption that even imperfect operations—that is to say, practically all operations—at any rate may and usually do lengthen life. The probability would seem to be, on the contrary, that they shorten it. There is absolutely no evidence to show that the usual series of operations do lengthen life, and the probability is all the other way. Hence the difference between a perfect operation, that extreme rarity, and an imperfect one, is not merely one of degree—that the patient dies of some other disease in the one case, and that his life is at least somewhat prolonged in the other. The truth probably is that the one operation lengthens life and the other shortens it: and very nearly all operations belong to the latter category. Mr. Childe tells us that, during the last seventeen years of his career, the surgeon Benedikt, of Breslau, gave up operating altogether in cancer of the breast, and the opinion of Sir Benjamin Brodie has already been quoted. These belong to a past generation, and the same surgeons, operating now, would doubtless obtain different results, because a certain number of their operations would be really adequate. But the overwhelming majority of operations now performed are essentially of the character of those performed by Brodie, and the probability is that their results are substantially the same as his—they do not even lengthen life, but shorten it.

Thus it seems probable that the only surgical operation which can really be commended to-day is the perfect one, which removes the whole of the disease; and this leads us, quite apart from any question of trypsin, to the formidable conclusion that practically all the operations actually performed for the removal of this disease are to be condemned. Observe that I speak not of the operations which *might* be performed, but those which in general *are* performed. It is not necessary to describe the average operation as "criminal," as advanced surgeons do: but their verdict may be noted.

No such condemnation applies to the various palliative operations which do not touch the tumor at all, and which therefore do not stimulate its growth and increase its malignancy. Such are the operations for making artificial openings in the intestine or the stomach, or for establishing short routes between various parts of the alimentary canal in order to avoid an obstruction. For some time to come such cases as these, plainly capable of being relieved without considerable risk by the surgeon, will continue to occur.

The general answer to this argument will be, however, that though imperfect operations may tend to shorten life indirectly by increasing the malignancy of the cancerous tissue which is left behind, yet the removal of a primary tumor of the breast or tongue may at any rate relieve the patient from much pain, from mechanical inconvenience, and also from the chronic blood-poisoning, not to mention the unbearable odor due to the growth of microbes in the tumor. To this reasonable argument I reply that trypsin and amylopsin can effect all these ends, not to mention far more. I have repeatedly seen trypsin abolish the pain of cancer altogether in cases

where morphine in large doses had failed, as it often does fail. Furthermore, the local application of these ferments dissolves away like magic the whole of the dead tissue which accumulates on the surface of an exposed growth. I say "like magic," and the results are only adequately so described; but of course there is nothing remarkable in the digestion of dead tissue by these two intensely powerful ferments; and the real wonder is that they have not regularly been used for decades past in order painlessly and certainly and completely to dispose of all the necrotic and decomposing and horribly putrid tissue which is so constant a feature of all exposed cancers—that is to say, of the very great majority of cancers at some period or other. This book will be read by many skeptics. To them I appeal on this point: whatever else they disbelieve, they know as well as I do—many of them knew it before I was born—that trypsin digests lifeless proteid matter. This involves no theory of cancer, and has, as such, nothing to do with cancer. They know, also, that the exposed surface of a cancer invariably dies sooner or later, and that the dead tissue undergoes bacterial decomposition, involving the production of blood-poisoning and unspeakable fœtor. The so-called "cachexia" of cancer, the loss of weight, the yellow skin and so forth, are now known to be largely, if not entirely, due to this accident, as it may be called, though it is an accident all but invariable. Will you not, then, consent simply to try the local application of trypsin as a digestive of *dead* tissue in these cases? In point of fact, the constant and immediate result—manifest in some degree within twenty-four hours—is the absolute disappearance of all the dead tissue, and the complete suppression of the fœtor. If trypsin did nothing

else, its introduction would be the greatest boon that has come the way of the cancer-patient since the introduction of the hypodermic use of morphine and antiseptic surgery.

As for surgical operation to relieve pain, I have never yet heard a patient complain of cancerous pain while undergoing trypsin injections under my direction. Nothing could be more remarkable or beneficent; but since I know that any treatment will cure any pain if only the patient believes that it will, I have never laid upon this fact the stress that it deserves.

Surgical operation, in order to remove a fungating and poison-producing mass, should now be no longer necessary. These features of cancer, including its odor, are no more known to those who employ the new treatment properly than are the pain and fœtor and foulness of surgery fifty years ago to the modern surgeons: competence in each case being assumed.

As strictly relevant to this question of palliative operation, I may here notice a case carefully watched by myself in conjunction with the responsible physician, to whom I referred the patient on her application after reading my articles in the *Daily Mail*. The case is recorded elsewhere by the physician in charge of it (*General Practitioner*, August 31, 1907.)

The patient, a woman, had had a cancer of the breast removed by a prominent surgeon at the Middlesex Hospital. The said surgeon need not be further particularized than by saying that his name was published as concurring in the adverse opinions on trypsin which came from that hospital in the summer of 1907, and as having been responsible for the patients on whom trypsin was tried.

The growth recurred, and the patient regularly visited the Middlesex Hospital and was seen by the surgeon who performed the operation. She had a large ulcer in the site formerly occupied by the breast, and this, when she came under the pancreatic treatment, was covered with a dark and fœtid necrotic mass. The supra-clavicular glands were involved, and there were several small growths in the skin. Had the patient belonged to another class of society, a second operation would probably have been performed in this case. As it was, the only treatment employed was the presentation of carbolic acid to the patient, with instructions to use it. I may remark in passing that few things in this whole business have appeared more lamentable to me than the fashion in which surgeons are wont to deal with cases that are past help from the knife. This patient suffered much pain: she was a typical example of cancer cachexia, and the odor of the growth—*or rather of the dead tissue upon it*⁴—was indescribable, and made her unendurable by herself or her friends. A palliative operation would have temporarily relieved her, though doubtless stimulating the growth. The application of carbolic acid to the outside of the necrotic mass did practically nothing, though in so far as it reached the living growth it would stimulate it according to Von Leyden's law.

Trypsin transformed that patient at once. The whole of the dead tissue was promptly digested away—as all dead tissue may always be digested away by trypsin, though even this necessary fact was not reported from the Middlesex Hospital—the horrible fœtor vanished ab-

⁴The odor of cancer is *always* due to this cause, which trypsin, of course, can readily remove. It might have been employed for this purpose ever since its discovery, now nearly fifty years ago.

solutely, and the patient's general condition was altered beyond recognition.

The treatment did for her, without pain or risk, everything that a palliative operation could possibly have done, and did so without stimulating the living tumor. Many observers have recorded similar facts; and to the surgeon or other critic who is prepared to deny all else, I would say, "Do you deny that an active proteolytic ferment can and must digest dead proteid tissue? If it can, as you know it can, will you not use it for this purpose in your advanced cancer cases?"

For the purposes of the argument it has been assumed by almost all the critics of my articles in Great Britain and the United States since March, 1906, that all patients suffering from cancer can be cured, or can at least have their lives prolonged by surgery: words like "criminal" and "brutal" and "irresponsible" have been freely addressed to me on the assumption that, in so far as my campaign succeeded, it would effect the death of patients whom surgery would otherwise have saved. Among the facts ignored have been the indisputable and everywhere admitted fact that the vast majority—certainly more than 99.9 per cent.—of cases are not saved by the surgery that is, however many might be saved by the surgery that might be. Worse than this, my critics have totally ignored the existence, at any given moment, of hundreds of thousands of patients throughout the world who are admittedly "past all surgery." In Great Britain alone, despite the surgeons, some thirty thousand persons die of cancer every year, and the number of cancer patients at any given moment has been variously estimated as at from sixty to one hundred thousand. Now of all these certainly the great majority are admittedly past all sur-

gery. Some of them have been operated upon once or oftener, some have delayed too long for any surgeon to undertake the operation, and a not inconsiderable proportion have been wholly inoperable from the first. A large proportion have been incapable of cure by operation from the first. Thus for tens of thousands of persons in every country in the world at any time all hope from surgery is over, and the number whom surgery can help at all is relatively very small, while the number whom surgery cures is all but negligible—it being remembered that I speak of actual surgery, and not of what might be if all surgeons were like the best and all patients applied at once.

This is to say that the argument from surgery is totally irrelevant to all but a minute minority of cancer-patients at any given time. The critics, without exception, have assumed not merely that the new treatment was worthless, but that the advocacy of a worthless treatment is equivalent to the injury of all cancer-patients. As a matter of fact, the most blackguardly and unscrupulous quack can only injure very few patients by robbing them of the hope of surgery, *actual* surgery having never had any hope for nearly all, and offering hope at a given moment to only a tiny proportion.

The actual fact is that the great majority of cancer-patients are without hope or help in the world except from measures other than surgery. It is commonly supposed, as it was by myself until last year, that cancer is a "surgical disease." But analysis of the facts shows that though surgery cures absolutely a tiny proportion of cases—say *perhaps* as many as 0.01 per cent.—the great majority of the remainder probably have their lives shortened by the surgery that is actually practiced. As for

the cases that are curable when they come up for treatment and would receive really curative treatment, I have yet to hear of a single one anywhere that was dissuaded from operation by my crusade and found trypsin and amylopsin wanting. I propose to defend myself without reserve or qualification, therefore, against the charge that I have injured any one whatsoever (except the surgeons) by my campaign, even though, in order to obtain a hearing for trypsin at all, I necessarily had to begin it when the treatment was in a very inchoate stage, and active injections were very difficult to obtain. On the other hand, I could print many grateful letters received from patients who at least were relieved of pain and foetor and cachexia.

The fact is, notwithstanding the splendid work done by a very few surgeons, that for the overwhelming majority of all patients in the present state of public information as to the early signs of cancer—the consequences of which Mr. Childe has so terribly demonstrated—and in the present state of surgery as it is actually practiced, there is no help in the world but morphine and the ferments, and no hope of prolongation of life or of cure except in the ferments alone. Those who have opposed this treatment, some honestly and others dishonestly, have deprived and are depriving all but very few cancer-patients of their sole hope: the substitute of surgery is of dubious value even where it can be employed, and is unemployable in the great majority of cases at any given time. In the absence of any possibility that patients will suddenly take to coming in time, and that surgery in general will suddenly reach the level of the best surgery, no words can adequately condemn those who are still prepared to deprive these patients of a mode of treat-

ment which offers hope, relieves pain, abolishes foetor and destroys all necrotic tissue without any risk or serious expense, even assuming that it can do no more.

In summing up, we may say that in the rare cases where a perfect operation might and would be performed—two distinct conditions—the patient should be operated upon. The operation involves some immediate risk to life, but it may accomplish at once what no other means can accomplish except in months, if then—and the use of the ferments is not excluded, though it is probably prejudiced, as I show elsewhere, by the operation.

But in that vast majority of cases where a perfect operation either cannot be performed or will not be performed, it is seriously to be questioned whether an imperfect operation should be performed at all. It involves immediate risk to life, it accelerates the growth of the malignant tissue which it leaves behind, and since a radical cure is in any case out of the question, life cannot be sacrificed by at least postponing the operation while the pancreatic ferments are given a trial. They will at least do all that the knife could do in such cases, not to say much more; and it is much better to employ them first, on the grounds I have cited, than to follow the procedure which, I do not doubt, many surgeons will still insist upon for some time to come, even in cases where they know that they cannot and will not effect a radical cure. This is to use the knife until it can be used no longer; and when the patient's strength is exhausted, when the disease has assumed a more malignant type, when the knife and the disease between them have destroyed various tissues and organs more or less necessary to life, the ferments will be employed. If, at this stage, they fail to save the patient—not having the power to re-create

new organs or tissues upon the ruins of the old—the surgeon will triumphantly point to the fact and cite the history of the case as proving that “there is no cure for cancer but the knife,” though the knife has had every chance and the patient lies dead before him! It is a brave argument, and its audacity gives it success at this very hour.

At the meeting of the British Medical Association in Exeter, 1907, there was a discussion on uterine cancer, which has much significance for us. Among the opinions quoted, it will suffice to take that of the great Italian gynæcologist, Pozzi, as typical. He denies that definitive cure of uterine cancer has yet been proved: “Even in the most favorable cases one can only speak of prolonged survivals”; and he has had only two such “prolonged survivals” in 204 hospital patients operated upon for cancer. Other surgeons have obtained much more favorable results, notably by means of the operation of Wertheim, who, however, has an immediate mortality of 20 per cent.—that is to say, one patient in five is killed by the operation, while one-tenth (11 per cent. is Wertheim’s own figure) are still without recurrence after five years: in other words, by the best known operation, one-fifth are killed outright, and an uncertain proportion of one-tenth are cured. The issue of the discussion was to insist upon the importance of early detection of the disease, and it was resolved that a committee should be appointed “to consider the best means of disseminating knowledge of the importance of the early recognition of uterine cancer.” But the fact for the present is that, in the actual state of things, surgery is all but out of court as affording a cure for uterine cancer; and, short

of cure, the probability would seem to be that its influence on the disease, as we have seen, is that of a stimulant.

At the same meeting of the B. M. A., Mr. Butlin, an unsurpassed authority, delivered the "Address in Surgery," which was devoted to the question of the contagion of cancer; and therein he insisted upon the risk, during operation, of infecting the wound with living cells. He says: "Cancers should not be cut into unless for diagnosis, and the wound should be tightly closed before the actual operation is commenced. The instruments which were used for the purpose of diagnosis must not be used again until they have been boiled. Exposed or ulcerated cancers should not be pressed against or dragged across raw surfaces made in the course of the operation. And care should be taken that breaking-down cancers are not opened during operation. If they are opened by mischance, means should be taken to cleanse the surface of the wound and to destroy the exuded contents of the cancer-cavity."

No one will question for a moment that, in general, these conditions are not complied with, and in the light of Mr. Butlin's researches there can be no doubt as to the result. This evidence tends, with all the evidence that has already been detailed, to the serious conclusion that the performance of surgical operation in cancer, apart from palliative operations which do not touch the growth at all, should be confined exclusively to those extremely early cases which, unfortunately, the surgeon so seldom sees. The necessary and warrantable demand of the surgeons for early cases is based on their demonstration of the deplorable results they obtain in cases that are not early, *despite the extension of their operations to a degree which involves a much larger primary mortality*

than the percentage of patients cured; the chances being often definitely higher that the operation will kill outright than that it will cure. Wertheim's operation, for instance, so highly praised, kills one in five at once, and cures less than one-tenth. This simply means, though the necessary inference is not drawn, that the overwhelming majority of the operations actually performed for cancer at the present day should not be performed. They are statistically shown to take much more life than they save. It is beyond comprehension that such results as Wertheim's, specially put forward as constituting a triumph for surgery—results which plainly assert, though apparently not plainly enough, that they take more lives than they save—should be quoted except in order to assert the only warrantable conclusion—that they should not be performed. If the best results take two lives in order to save one (Wertheim has a primary mortality of 20 per cent. and 11 per cent. of "survivals" for five years), we may estimate the value of the results obtained by the surgery of cancer in general.

I am at a loss to conceive how any one, surgeon or layman, can look at such figures as these without admitting that, if any conclusion at all is to be drawn from them, it is that, of all operations for cancer at present performed, only a minute proportion are legitimate. The most radical and recent operations for uterine cancer, for instance, are self-confessed to be a gamble for life or immediate death, with the chances very heavily in favor of the latter; and the considerations advanced by Von Leyden and Sir James Paget and many others suggest that death is hastened by the operation in the case—to take a current instance—of the seven-tenths of patients who remain, when two-tenths are accounted for as killed

outright, and one-tenth as free from recurrence after five years. And we are dealing, be it remembered, with the rare surgeons here and there, who can operate on only a tiny proportion of all cancer-patients, *and who choose their cases.*

Until, then, the actual facts as to the quality of the operations performed, and their date relatively to the onset of the disease, are utterly revolutionized, we cannot avoid the conclusion that very nearly the whole of the surgical treatment of cancer, as it is actually practiced to-day, is illegitimate and should be suspended.

In its place there is here put forward a mode of treatment by various cancrotoxic ferments, which, in its various forms, has already achieved many carefully recorded successes even where surgery has failed, can and does habitually accomplish, when properly practiced, immense palliation of the disease in all its most distressing aspects, *and has no primary mortality whatever.*

The present volume is written on my own responsibility, notwithstanding the indispensable help I have incidentally received from Dr. Beard. He is not to be credited or discredited with anything in it that is not directly attributed to him. It is necessary to say that the views expressed in the present chapter by no means entirely meet with his approval. He insists that, since nature does not operate upon trophoblast, and permits it to grow for only seven weeks at most before she begins to attack it—in the case of man—our business should be to reproduce nature's method as closely as possible. In the light of Von Leyden's work he is more strongly convinced than ever that surgical operation, in general, affects a tumor in such a way as gravely to complicate,

if not to make impossible, the reproduction of nature's method in dealing with trophoblastic tissue. He maintains that it is impossible to do more than demonstrate nature's method, and that if this for success requires certain conditions, it is not the fault of the therapeutic method, which he advocates on the model of the natural method, that it demands similar conditions for success. Thus, apart from purely palliative operations, such as the making of artificial openings in the bowel at a distance from the disease, Dr. Beard would limit the function of surgery entirely to the removal of the remains of dead tumors killed by trypsin, the irritation of a living tumor by the knife being regarded by him as an artificial disturbance which renders invalid the attempt to reproduce nature's method of dealing with malignant tissue, which normal trophoblast unquestionably is. He believes, and the opinion is shared by Dr. Cleaves, whose experience is large, that recurrent cases—*i.e.* cases already modified by the knife—are not really suitable for the new treatment. Not a few of such cases have been reported cured by it, and many more vastly relieved and their fatal advance arrested or retarded; but Dr. Beard will not lay much stress upon them.

At present, however, the treatment has been practically confined—and necessarily so—to advanced and recurrent cases, often many times recurrent. I personally cannot take upon myself the responsibility of counselling the refusal of operation in such rare and early cases, uncomplicated by secondary growths (though no one can ever be sure of this), as do occasionally come before the surgeon. I believe that I have shown good reason, derived largely from the mouths of surgeons themselves, why operations upon the disease *in all other cases—i.e.*

certainly not less than 99.9 per cent. of all operations—are to be condemned and should be abandoned. There remain, as offering a difference of opinion between Dr. Beard and myself, only the very rare cases in which the surgeon honestly and unreservedly believes that an operation can (not *might*) be performed—and more, that he will actually perform this operation on this occasion—which will radically extirpate every portion of malignant tissue in the patient's body.

I do not regard this question as a serious one, for there are not a few early cases, if the whole of civilization and the lower animals be included, in which the patient for some reason or another declines to be operated upon, or, as in animals, may be legitimately experimented upon. No such early and favorable case, so far as I know, has yet come under the competent, or even the incompetent, performance of the pancreatic method of treatment. It has had to establish its claim to a hearing by means of cases abandoned by the surgeons after one or many operations; but early and primary cases, where the patient refuses operation, or is an animal, will doubtless shortly come under the treatment, and the results should speedily and finally settle the question.

CHAPTER XII

THE PREPARATION OF THE FERMENTS

WE must now consider a practical matter of great complexity which may seem, and did at first seem, to be very simple. This is the preparation of pancreatic ferments for purposes of injection. They are contained—or at any rate their immediate antecedents are contained—in any conveniently obtained pancreas, such as that of a pig or an ox or sheep. From the pancreas of such a recently killed animal active digestive solutions may be prepared by means of glycerine. It might be thought, then, that no more was necessary than to make such solutions, sterilize them, and seal them up; nor was any great difficulty offered by the fact that sterilization by heat was inadmissible, since this destroys the digestive power of trypsin. There is no difficulty in obtaining material, nor in making clear solutions and sealing them up in neat little glass phials. Unfortunately, however, more than this was necessary. Powerful though these ferments be, they are also delicate. One of the chemists who have worked at this subject has compared trypsin to dynamite, with the comment that the comparison really does poor justice to trypsin. Indeed, the digestive power of this substance, involving no loss of its own power, has long been one of the standing wonders of chemistry; but yet it demands a nicety of conditions in which to work or even to retain its possibility of action. These

facts were not fully realized at first, and even when the difficulties were realized by some workers, they were too commonly thought to have been overcome when they really were not. Let us now look at the facts which rendered necessary a much closer study than had hitherto been made of the conditions under which these ferments may be prepared for use.

In critically comparing all the results that have hitherto been obtained, we have found ourselves compelled to observe certain anomalies, the explanation of which was not forthcoming. It might quite well be expected that certain kinds of cancer, those for instance which are known to grow more slowly, would yield more quickly than others to treatment by the pancreatic ferments; but no such general result was to be observed. The response to the treatment bore no definite and absolute correspondence to the type or the previous history of the growth. Indeed, it was found that when the treatment, apparently constant, was applied in various cases which, so far as could be observed, seemed to be precisely similar, the results obtained were quite discrepant: whilst in one case the tumor responded at once and most satisfactorily, in another the injections might have consisted of salt solution and nothing more so far as any observable results were concerned. All the chief kinds of tumors have, at one time or another, shown response to the treatment—a point which is evidently of the greatest importance. But they have by no means always shown the same response, or, indeed, any response at all. Furthermore, while one observer has obtained results within a few weeks, another observer, working upon cases apparently identical, and giving doses that purported to be the same, has had to wait many months.

PREPARATION OF THE FERMENTS 139

There were and are, of course, certain details, already noted, which would go a long way to explain these anomalies. There were, first of all, the practitioners who did their work in what, not to put too fine a point on it, must be called a dirty fashion: whether by ill-luck, such as may sometimes attend any one, or by carelessness, their injections were followed by local symptoms which would suggest that Pasteur and Lister had never been born. Notwithstanding the experience of the Middlesex Hospital, nothing more need here be said as to the production of abscesses by the injections, for the experiences already published abundantly prove that these should and need never occur.

Then, again, there were the practitioners who, quite excusably ignorant of the delicate nature of the ferments, neglected to cool the hypodermic needle after boiling it, or failed to wait for the cooling of the water with which the injections are diluted, and which, of course, must first be boiled so as to render it sterile. If the ferments be heated above only $60-65^{\circ}$ C., they are rendered absolutely inert.

Nevertheless, when all these sources of failure were excluded, the anomalies to which I have referred still remained. It became necessary, therefore, to begin at the very beginning, and to discover the facts of ferment solutions in general.

These facts have been startling enough. The various firms of chemists who now supply these ferments in the form of injections for the treatment of cancer are quite above suspicion as to their probity. They doubtless all use the best methods known to them, and use them with the most scrupulous care. Nevertheless the results which they obtain are in some cases singularly unfortunate, as

we shall see. Furthermore, let us note that if such results have been obtained by all but one of the best firms, we need not look far ahead in order to prophesy that very soon, when firms all and sundry enter into competition in this matter, the market will be flooded with preparations that are simply worthless. Quite sufficient harm has already been wrought in this way. In the first place, many patients have failed to find relief because, as we shall see, they were undergoing the pancreatic treatment only in name. More serious still, because of its wider results, is the fact that these failures and abortive experiments are in some cases recorded, with the result of gravely discrediting the treatment and delaying its general acceptance. It is absolutely necessary, as we shall see, that we should demand a quite new series of requirements before undertaking the prosecution of this work.

Lately there have been conducted, first in New York, and later also in London and Berlin, a large number of chemical experiments with the pancreas gland, as to the mode by which its ferments may be best extracted from it. At the same time there have been in process a large number of observations upon the actual digestive activity of the various preparations that are already upon the market. Lastly, a great deal of work has been done in the attempt to ascertain how long these various preparations will retain their activity, assuming that they possessed any to begin with.

In the first place, then, we have found that various preparations stated—quite honestly, of course—to contain such and such a percentage of trypsin or amylopsin, or both, may differ in their activity in ratios actually so high as that of 1 to 500. This is to say, that two injec-

tions supposed to be identical may actually differ so much that five hundred drops of the one will be required to digest the same amount of milk as will be digested by one drop of the other. Now this is a very easy fact to state, but let any reader consider for himself what it signifies in practice. It means that if the dose of the more active preparation be adequate, that of the other is only one-five-hundredth part of what it ought to be. This is as good as to say that the use of the second preparation is an expensive, painful and fatal farce. Ferment injections, of which no more may be said, are being employed at this moment, I cannot doubt, here and there, in all parts of the world, and especially in Great Britain.

It is not quite clear how it is that, in the course of making their preparations, certain manufacturers, even though they use fresh pancreas-gland and extract the ferments from it with glycerine in a perfectly correct fashion, manage somehow to reduce their work to worthlessness by the time the injections are sealed up in the little glass phials in which they are dispensed. There the fact remains, however. The same remark applies to preparations made from trypsin in powder. Some of these will be found to be highly active; others, even in concentration, will effect no change in dead milk in an hour. Evidently it is a sorry business attempting to cure cancer with such. I strongly believe that no injection made up from trypsin in powder is desirable.

We must find in the first place, then, some accurate and certain means—simple if possible, but at any rate accurate—of determining the activity of any given injection. This has now been done. I am anticipating the publication of this work in the scientific journals, but I have been doing so all along with the full consent of the

original workers and for the best and most obvious of all possible reasons.

Amongst the papers presented to the Royal Society by the late Sir William Roberts, of Manchester, who, until his death a few years ago, was the greatest living authority on digestion, was one in which he showed that of the various means which may be employed for estimating the activity of the digestive ferments, the best is what he called the meta-casein test. At the time when his work was done, not even the wisest could guess the importance which it would afterwards assume; but there is no sterile knowledge in the whole realm of things, and this is now bearing fruit. The test in question depends upon certain observable changes wrought by the digestive ferments in the chief proteid of milk, which is known as casein.

For purposes of accuracy it is necessary, in the first place, to obtain a standard milk, and that which has been employed is what we may call London County Council milk, which contains the 4 per cent. of proteid demanded by that body. To a fixed quantity of this milk, under fixed conditions of temperature, there is added a fixed quantity of the ferment preparation that is to be tested, and the time it takes to change the milk completely is then precisely noted in minutes and seconds. Whereas one preparation, diluted ten times, will produce the meta-casein reaction in perhaps forty-five seconds, another, undiluted, will effect nothing that can be observed in an hour.

Sir William Roberts, as was his fashion, went thoroughly into this matter. He provided a convenient formula whereby the result of such experiments can be expressed in units of digestive activity. The mode of con-

PREPARATION OF THE FERMENTS 143

struction of the formula is immaterial here. It is comparable to the formula employed, as many readers will know, for estimating the activity of the diphtheria antitoxin. In that case it was soon found impossible to make any progress so long as the strength of injections was expressed in terms of what was put into them. In a case like this we must express the strength of an injection not by what we put into it but by what it does. The business of the diphtheria antitoxin is to neutralize the toxin or poison of diphtheria, and so the dose is now expressed in units of neutralizing power. Similarly, the business of the digestive ferments trypsin and amylopsin is to digest, and therefore the proper mode of expressing the quantities employed would evidently be in units of digestive capacity. This digestive capacity is "D" in the formula of Sir William Roberts, and this mode of numeration is as superior to that as present employed as science to vague opinion. Observe a proof of this superiority. Two injections, both honestly prepared, may purport to be identical. Subject them to this new mode of description, and whereas the value of one is found to be 500, the value of the other is found to be 0.7—these figures referring to digestive capacity, which is, of course, the vital matter, and the only vital matter, in this connection, apart from the possible existence of poisonous peptones in the injections.

Very plainly, then, we must make a new demand of the chemists, and this is simply that, just as they have standardized their preparations of other drugs, so they must standardize their preparations of these ferments. When a doctor prescribes five drops of tincture of nuxvomica, he knows that this will always contain a certain definite quantity of strychnine, and so in other cases;

but I know of no other case in which the importance of this principle of standardization can be compared with that of the case we are now considering. The chemist must standardize his ferments, and when that is done, the public and the profession must absolutely ignore all preparations which, while professing to contain this and that proportion of the ferments, are not standardized. The stated proportions of the ferments may very well have been put into the preparations, but if they are now incapable of digesting milk in months, it is not well to expect them to cure cancer.

When this most necessary advance has been achieved, we can begin to attach some significance to the reports of those workers who fail to obtain the results they desire. Furthermore, we shall then be able to attack the question of dosage, which has hitherto been in a state of chaos. Obviously we cannot come to any agreement if we imagine that 20 drops of a 5 per cent. solution of trypsin always means one and the same thing, whereas 20 drops in one case may really be equal to 10,000 in another.

Here I may quote certain of the results obtained from examination at various dates of four sets of preparations put upon the market by the four firms which, in April, 1907, alone supplied them. As the table shows, the preparations were examined at three different dates, and it will be seen that in nearly every case experience wrought considerable improvement in them—that is to say, preparations issued at later dates were more effective. I only wish I could give the names of the firms, but that is not really necessary, since it is now to be expected that no practitioner will employ anything but definitely standardized preparations. The figures are

PREPARATION OF THE FERMENTS 145

units of digestive power. The letter T refers to units of tryptic power, and the letter A to units of amylolytic power. As regards the former, two methods of estimation were employed, and their discrepancy in certain cases shows how difficult and complex this question is—even the metacasein test being doubtful.

TABLE

<i>April, 1906.</i>	<i>February, 1907.</i>	<i>April, 1907.</i>
1. T = — A = 0.0 T = 11.2	T = 9.6 A = 0.7 —————	T = 20.8 A = 8.3 T = 20.8
2. T = — A = 62.5 T = 22.3	T = 250 A = not taken —————	T = 250 A = not taken —————
3. T = — A = 250 T = 22.3	T = 500 A = 200 —————	T = 500 A = 200 T = 166.6
4. T = — A = 0.0 T = 5.6	————— ————— —————	T = 50.0 A = 7.1 —————

A glance at the above table will show how markedly the various preparations differed even after a year's experience. In the case of the most active one, No. 3, the firm made comparatively little improvement so far as the amylopsin was concerned, but so far as the more important trypsin was concerned, it apparently multiplied the activity of its injection by 8. Even as late as April, 1907, injection No. 1, of which I may at any rate say that it has been very largely employed in Great Britain, was extremely feeble, and could not be expected ever to effect a cure. Of the preparations examined, only Nos. 2 and 3 can be regarded as substantially useful.

Now let us turn to another question which, though

much less important, is at any rate of considerable interest for the patient. At one time it was supposed that the injection of trypsin in a plain salt solution would cause no pain whatever beyond the mere prick of the needle. This appears, however, to be not so. It would seem that, even when trypsin is so injected, the difference between the specific gravity of the solution and of the blood is sufficient to cause local disturbance. Solutions of the ferments are always of very high specific gravity. Beyond this there is the fact that these ferments will not keep in clear salt solution. More serious, however, from this point of view, seems to be the glycerine which is necessary for the preservation of the ferments. Earlier preparations actually contained as much as 85 per cent. of glycerine, and 20 per cent. seems to be the present minimum. The attempt to substitute thymol was found to cause more pain than ever. Worse than this, free acetic acid, with which the pancreas is treated in order to convert its trypsinogen into active trypsin, has actually been found in some of the injections, and that, as every student of drugs well knows, is one of the most painful and powerful of local irritants. The addition of a very little bi-carbonate of sodium to the solution will neutralize the acid; but if this be done the most rigid aseptic precautions must be observed. On no account must carbonate of sodium be added, which promptly destroys these, like most other ferments. The best of the most recent injections, however, contain no free acetic acid. For the greater part of the time that this treatment has been in employment, it has been necessary to dilute the injections with water in order to lessen the pain caused by the glycerine which they contain.

As we have seen, this dilution entails requirements as

to sterilization and cooling which have too often not been met. It is therefore good to be able to state that the best of the newer injections require no dilution. Both Messrs. Fairchild Bros. & Foster in New York—our indebtedness to whom from the very first cannot be overstated—and Messrs. Squire in London, appear to have overcome this necessity. The solutions are still liable to cause pain in some cases, however, since it has not yet been found possible to dispense altogether with the irritant glycerine.

At any rate I make the formal statement of the necessity for the standardization of the preparations that are put upon the market. If one firm can comply with this requirement, so can others. It is to be hoped that before long the chemists will be able to do the work which still remains, so that we may have upon the market preparations which are sterile, will keep for considerable periods, are neutral in reaction, contain no irritating substance whatever, and no poisonous peptones, require no dilution, and do just so much work as they profess to do, neither more nor less.

This question of keeping is obviously of considerable importance, and too little attention has yet been paid to it. The making of preparations from commercial trypsin in powder is a most unsatisfactory proceeding, since this is apt rapidly to lose its efficiency. The systematic testing of preparations after they are made always shows that this method is of little use. It was employed by Von Leyden. But no less importance attaches to the keeping of preparations even after they have been tested and found satisfactory. We must entirely condemn on this account the supplying of preparations *in bulk*. Quite apart from the question of keeping, intermittent exposure to the air is involved in this case, and condemns the

method. One dose in one closed glass phial must be the rule. On this point Messrs. Squire & Sons supplied to the *Chemist and Druggist*, January 5, 1907, the following useful note:—

“If it is intended to distribute a solution throughout the trade for the purposes of stock, such solution would be useless unless it would remain unimpaired for a year or more; but if it is intended to be supplied, either direct to the doctor, or through the chemist, for immediate use, the necessity for keeping such a long time does not arise. The pancreatic ferments retain their properties better in very strong glycerin menstruum than in any other medium, but such solutions have drawbacks not shared by others. They must be diluted before use with sterilized water (which takes time), and even then have a tendency to cause pain and inflammation when injected, and have other serious disadvantages. For these reasons it has been Messrs. Squire & Sons’ practice to prepare solutions which are intended for practically immediate use, and they have no complaint of the drawbacks they have indicated; but these solutions are not intended to be put away on a shelf or in a cupboard and brought out again for use in six months’ time or a year, under the impression that they will have retained their full activity. Ferments are such delicate substances that every precaution should be taken to prevent change of their physiological as well as of their chemical nature.”

It seems that even the latest preparations, even when kept under the best conditions, do not retain their activity indefinitely or anything like indefinitely, and probably one month is the limit of practical utility after a preparation is made.

As regards hot climates, difficulties will be encountered

PREPARATION OF THE FERMENTS 149

which are very nearly insuperable, so far as sending out preparations made in England or the United States is concerned. At as low a temperature as 120° F. the activity of these preparations begins rapidly to diminish, and I am told that the temperature of the hold of a ship in the Red Sea may often be as high as 120° to 130° F. It would seem to follow inevitably that the only practical means, so far as the treatment of malignant disease in the tropics is concerned, will be to have the preparations made there. I would emphasize this point, as my advice has more than once been asked as to such cases. A similar difficulty applies to Australia, and it is rather doubtful whether the sending of preparations across the Equator can be of the smallest use, though the Fairchild preparations have done good work, it is said, in New Zealand and even in Benares.

One practical moral of these facts as to the keeping of preparations is that not merely must only standardized ferments be employed, but also the practitioner must introduce the additional safeguard of making at least some rough test of their activity when he employs them, if only by adding specimens of the trypsin injection to milk, and observing the bitter taste which is produced by its digestion; and, in the case of amylopsin, by the easy and striking test with starch and iodine. Tincture of iodine, for instance, added to starch produces a deep blue color, due to the so-called iodide of starch. The previous treatment of the starch with the amylopsin preparation at the temperature of the blood should render the production of this coloring impossible. I have previously suggested that the practitioner would even do well to test, not the injections from the phials direct, but the material which he has already drawn into his syringe, and which he is

about to inject. For all may be well with the preparation until the phial is broken, and there may be a slip, so to speak, even between the cup and the lip. This suggestion was the more necessary when the preparations required dilution, but it may be necessary even now should the practitioner sterilize his syringe by heating it and fail to wait until it is cool enough before he employs it.

Here it would be well to describe very briefly one, at any rate, of the sound methods which are now employed in the preparation of these ferments. Pigs are the animals chosen, their health being certified by the official inspector. The pancreas-glands are collected and are acted upon within, at the latest, four hours. But even here an important point arises. The fact has for some time been known that the character of the pancreatic juice is capable of considerable modification. Says Prof. Moore (*Recent Advances in Physiology and Bio-Chemistry*, p. 193) :

“When an animal is kept for a long period (some weeks) upon a definite and constant diet, the ferment content of the pancreatic juice becomes adapted to the character of the food. If, for example, an animal which has been fed for some weeks entirely upon bread and milk is brought on to an exclusively meat diet, which in contrast with the other diet contains more proteid but scarcely any carbohydrate, it is found that the power of the pancreatic juice for digesting proteid increases from day to day, while the digestive power for starch progressively diminishes. On reversing the diet again to bread and milk, similar but inverse changes are observed.”

PREPARATION OF THE FERMENTS 151

Hence even the feeding of the pigs whose pancreas-glands are employed is a matter of practical importance. I return to this point when discussing Prof. Bier's results with the ferments of pigs' blood.

We must note further that the various preparations of amylopsin that have been put upon the market differ as widely in their powers as those of trypsin. The test of activity in this case has been already referred to. Here also the activity of the preparation can be expressed in units of digestive power, and beyond a doubt preparations of this ferment also require to be standardized.

Lastly, let me add that no one who has any acquaintance at all with the facts of these ferments can possibly pay any attention whatever to negative results that may be published, in which the activity of the ferments employed was not formally demonstrated, and that in specimens taken at the last possible moment.

I would devote the last part of this chapter to a series of definite recommendations to manufacturing and dispensing chemists regarding the preparation and distribution of these ferments. The various competing firms, some of whom are doing and have done terrible harm despite their good intentions and efforts, must renounce altogether solutions for injections of such ridiculous strengths as 2 and 5 per cent. It was the employment of such injections that brought discredit upon the treatment in its early stages. Quinine cures malaria, but quinine in doses of, say, one-hundredth of a grain will not cure malaria. These ferments are being supplied and used in doses just as irrelevant to the needs of the case. The manufacturing chemists must put an end to such doses by ceasing to supply these absurdly weak solu-

tions. Furthermore, I would counsel them to cease altogether to describe their preparations as consisting of such and such percentages of trypsin or amylopsin. They must employ the means which already exist of standardizing their preparations. The firms which cannot make preparations of adequate strength and are unable to guarantee in definite figures the activity of what they do make, may be counseled in the name of humanity to leave these ferments alone altogether, and confine their energies to aloes or cold-cream. Yet further, I make the demand that every box containing these injections must have stamped upon it the exact date of manufacture, with a further statement printed on the outside of the box, so that doctors, nurses, patients and friends may see it, that the contents are not to be used on any account later than, say, one month after the date of manufacture. It should also be added that the estimated and stated activity (of the present preparations) undergoes a rapid decline from the very first day. Messrs. Squire & Sons of London have marked every box supplied since the beginning of the present year with the date of the preparation of the solution. The initials of the responsible chemist are also added, and the facts of each box can thus be ascertained on reference. This is a most excellent example which must become the rule.

In my opinion all this is absolutely necessary in the present state of the practical chemistry of the subject. It will increase the expense of the treatment, but injections which have lost all their activity are dear at the price of dirt, and active ones may prove worth their weight in life. Yet further still, with the injections must be supplied prominent warnings as to the effect of heat (and, I should expect, of exposure to light); and, lastly,

PREPARATION OF THE FERMENTS 153

I place no trust in the supply of injections in bulk either to doctors or to dispensing chemists. If the precautions I have formulated are attended to, it will be impossible for chemists to take in a stock of these ferments and rummage for them among their shelves as they are required. The place for injections that are not quite new is not the blood of living men, but the dustbin.

Parallel suggestions may be made to practitioners. It is possible for them, if they please, to compel the manufacturing chemists to comply with these requirements. I would warn them against old injections, 2 per cent. injections and the like, and against any one who offers them trypsin but no amylopsin: I would warn them against the use of heat at any stage in their technique, and against the purchase of any solutions in bulk. The pioneer chemists in the preparation of really efficient injections are Messrs. Fairchild Bros. & Foster of New York (London agents, Burroughs, Wellcome & Co.), who have, of course, for many years been the pioneers in the study of the digestive ferments. They will offer the practitioner trustworthy and extensive information as to chemical details. The only other firm of manufacturing chemists with whose preparations, so far as I know, any really satisfactory results have been obtained, are Messrs. Squire & Sons, 413 Oxford Street, London.

I fully realize the responsibility which attaches to the writing of this chapter, and at the risk of tedious reiteration I must return to certain points already discussed. It is my desire completely to suppress, if possible, the injurious activities of various firms whose preparations are worse than worthless, and whose number will doubtless soon be added to. Even as I write I receive a specimen capsule of the (asserted) tryptic strength of 2 per cent.

from a famous firm which has not hitherto entered this field. I only wish that in dropping it into the waste-paper basket I could dispose of all its like. But, on the other hand, there is the risk that, in the effort to put a stop to the sale of rubbish, I may hamper the firms—of which, so far, I know only two—whose preparations are of real value, and it is in order to avert this result that the following observations are made. In the winter most of them may be ignored, but in the hot weather the difficulties, even of the pioneer manufacturers, are greatly increased, and it would be most disastrous were I to multiply them by demanding the impossible.

In the first place, as regards the question of dilution, we must observe that possibly an injection which does require dilution at the moment of injection may ultimately prove to be the best adapted for the purpose, the most potent, and the best in “keeping” qualities. Against such advantages the mere trouble of making the dilution would not weigh for a moment. My objection to dilution, however, has no reference to the trouble of making it, nor to the slight additional time involved, but solely to the risk of introducing microbes which may cause abscesses. This is, perhaps, the least important of the risks involved in the whole matter. It is nothing at all to the real risk, which is that of using useless material; and the competent professional reader may well accuse me of rating too low the skill even of the least skilful practitioner. It is by no means proved, indeed, that the abscesses which have occasionally followed injection were due to the dilution. Experience borrowed from ordinary surgical procedure would direct us rather to criticise the cleansing of the doctor’s fingers. Indeed, it is only because the new treatment has had to fight against such

incredible ignorance and prejudice that I have been compelled, not only here but in my various articles, to take this question of abscesses so seriously. I have had to fight the belief that trypsin itself causes abscesses. Perhaps at this stage, however, it might suffice to dismiss the matter in a word and take the elementary facts of abscess-production for granted. There is no more inherent necessity to do otherwise in this case than there is for the surgeon who describes a new form of operation. In this matter, however, we have had every kind of factitious and unnecessary difficulty to encounter. Our case has been that of the surgeon who, describing a new operation, should be informed that the operation has been tried, that the wound became septic, and that therefore the operation is a failure and he a fool. Then, as has been observed to me, to talk of the risk of using too hot water in diluting the injection is as if one should talk of the risk of an operation by cutting into the wrong place; and I admit the force of the analogy. But in advocating this treatment I have all along had to fight just such arguments.

Thus the manufacturing chemist, whose difficulties are far greater than those of the doctor, is surely entitled to say that he declines to take all sorts of chances as to the stability and activity of his injections merely because there is a risk that some doctor may not make the dilution properly. Such a doctor should leave the treatment of cancer to persons of ordinary skill, and should confine himself to, let us say, spraying insecticide solutions upon rose-bushes.

We are only at the beginning of this matter. It may conceivably appear that the use of an injection diluted much beyond any hitherto used may be the best pro-

cedure; and in that case my demand for injections which require no dilution is simply a hindrance to progress. Evidently, if of two injections equal in digestive potency but unequal in volume, the bulkier is the more readily diffused and absorbed, that is the better; and it may be that the chemist is unable to supply in a stable form so dilute an injection. In such a case the dilution would have to be made at the time of use, and ordinary competence on the doctor's part would have to be assumed.

During hot weather it is possible that stable injections requiring no dilution—that is to say, already diluted—cannot be prepared; or it may be that injections requiring no dilution can be prepared, but that they will become turbid in a few days. The manufacturer is compelled to avoid this result, even though he may know that the turbidity indicates no diminution in potency, and that the injection is still sterile. He cannot give instructions to filter the injection and use the filtrate, though that would be quite satisfactory in an ideal world. It would not “work” in this world. Hence he is compelled, perhaps, to supply injections which require dilution. If the practitioner will not use such injections the manufacturer's only alternative is to supply weaker injections. Perhaps the reader will now begin to realize the nature of the difficulties involved in this subject, and also the difficulty of the writer, whose duty it is if possible to make demands which will suppress the irresponsible purveyor of useless preparations, while at the same time doing everything possible to facilitate the work of the conscientious manufacturer, without whom nothing can be achieved at all.

On returning to London after a short holiday in August, 1907, I was informed of a case new to me, which

was under the supervision of my friend, Dr. Meggitt, whose results are noted elsewhere. Here, for the first time in his experience, which began the day after the publication of my article in the *Pall Mall Gazette* last December, the treatment seemed to accomplish nothing at all, notwithstanding that the case was relatively favorable, though long past all surgery. The doctor in charge was keeping his injections in ice during the warm weather, and Dr. Meggitt's question to me was whether this might account for the failure. Certainly it might. Some years ago, Prof. Bayless of University College, London, showed that trypsin in solution soon becomes inert at the freezing-point of water, or 0° C. So here is yet another pitfall which, but for this accident, fortunate enough for all but the patient, I should have omitted to mention. I believe that some firms of manufacturers, unacquainted with the facts, have actually recommended practitioners to keep their injections in ice during hot weather, and this direction was being followed in the case in question. It is thus likely that the risk of heat, insisted upon, as we are bound to do, will tend to the similar risk of cold. Ice may, of course, be applied to the skin after injection, though that is no longer necessary; but injections must not be kept in ice in any weather, either by the manufacturer or the chemist (who is better without any injections to keep) or the practitioner. This fact regarding trypsin, which is thus perhaps more difficult to keep than any drug in the Pharmacopœia, or any kind of food, makes more unmanageable than ever the problem of sending it to or through hot countries, or of manufacturing it in them. I am glad to be able to warn the highly conscientious and scrupulous practitioner

against a risk to which he especially would otherwise be liable.

It is evident that a patient gets the same dose of medicine whether he takes it "neat" or with water; and similarly a given dose of trypsin is taken whether water be taken with it or not. In other words, a dose of given tryptic potency will presumably have just as much therapeutic value when administered in a hundred minims or drops as in twenty.

I repeat what cannot too often be repeated, that the whole matter is still in the early stage, notwithstanding the magnitude of the results already achieved. It has yet to develop, I do not doubt, no less than antiseptic surgery has developed since the late 'sixties. We know practically nothing yet as to the relative value of various kinds of injections any more than, to use a loose analogy, Lord Lister knew in 1868 of the relative value of various antiseptics and antiseptic methods. We have yet to differentiate between injections containing trypsin in its normal associations with other pancreatic products, and injections containing large proportions of amylopsin; and we have yet to discover what, on theoretical grounds, I think there may be,—an ideal proportion that should exist between the two ferments in every injection. I believe that the present method of using injections rich in trypsin at first and injections rich in amylopsin later is merely a rude device for immediate needs. If cancer would hold its hand for five years we should not need to adopt such methods. But it is evident that, on Dr. Beard's theory, there must be a certain amount of amylopsin which is required to complete the digestive processes initiated by any fixed quantity of trypsin in average circumstances, and this proportion must be ascertained. I say "in

average circumstances," because we must not be deluded into thinking that a given quantity of a ferment can only do a finite quantity of work, as a given quantity of an acid will only neutralize a definite quantity of alkali. When we can arrange all the conditions, a given quantity of a ferment will do an infinite amount of work. This is one of the standing marvels of ferment action. But amongst the many factors which we cannot arrange as we would, at any rate at present, in the case in question, is the factor of time. We know nothing as to *how long* a dose of trypsin remains in contact with the substance of a tumor, little as to whether, after a time, it is removed through the venous or lymphatic circulation, nothing as to whether acid or other substances in the tumor may render it inert after a time, nor how long that time is, nor what factors determine its length, nor how those factors vary. The all-important first step has been taken by Dr. Beard, but there remains work for many a year to come. We must remember that chemically pure trypsin has never yet been obtained anywhere, and that, for all we know, half a dozen ferments, each with its own specific powers, may be included under what we call trypsin. There is magnificent work yet to be done by the chemists in this matter; and fifty years hence our successors and those of us who, like the writer, may not unreasonably hope to be still working, may wonder that any results at all were obtainable in the present quite rudimentary state of our knowledge.

CHAPTER XIII

THE DETAILS OF TREATMENT

I PROPOSE in the present chapter to discuss as fully as possible everything that has at present been ascertained as to the best means of carrying out the pancreatic treatment of malignant disease. By this term I include not only cancer, but also sarcoma. These two chief forms of malignant disease cannot be regarded, from the present point of view, as in any way fundamentally distinct. I confine myself to the pancreatic ferments, not as begging the question of their superiority to other ferments, but simply because I believe them to be, at any rate, the most useful at present generally available.

It is hardly necessary to say that these directions are not intended for the public at large, but for responsible physicians. No more than the details of antiseptic surgery can the details of this treatment be carried out by any one but a trained physician.

The first necessity is to obtain suitable preparations for use. In this respect there are several competing firms of chemists. At one time or another it is probable that nearly all of these have in good faith offered for sale preparations which were of no utility. At the time of writing, such preparations are certainly upon the market, and are, unfortunately, being used. Furthermore, there are in use preparations which, though not entirely inert, are far too weak to be of any real use, and within

such a category fall 90 per cent. at least, I am assured, of all the injections that have hitherto been employed.

At present there can be named two trustworthy firms between whose preparations it is not possible to make any choice at this time. One of these has its headquarters in New York, and the other in London. Physicians and victims of cancer are greatly indebted to both of them for the long and expensive researches which they have successfully undertaken. The actual pioneers in the production of effective preparations were undoubtedly Messrs. Fairchild Bros. & Foster, Fairchild Building, Laight Street, New York City. It will be familiar to many readers that for years past this firm has specialized in the preparation of the digestive ferments for medical purposes, and their long experience has unquestionably been of the utmost value to the new treatment. Undoubtedly, a part explanation, though by no means the whole, of the fact that results were obtained in America at a date relatively so early is to be found in the fact that Messrs. Fairchild's preparations were exclusively, or almost exclusively, used across the Atlantic from the first.¹ But until the present year, if not still, the best preparations obtainable in Europe were also Fairchild's, *deteriorated inevitably* by their transatlantic journey.

The English firm which has contributed to the per-

¹London Agents and Foreign Depôts of "THE FAIRCHILD PREPARATIONS":

Burroughs, Wellcome & Co., Snow Hill Buildings, London.

Burroughs, Wellcome & Co., 14 Via Carlo Alberto, Milano, Italy.

Scott & Co., 4 Rue Chauveau-Lagarde, Paris, France.

E. Nadolny, Spitalstrasse 9, Basle, Switzerland.

Ch. Delacre & Co., 50-52 Rue Coudenberg, Brussels, Belgium.

Linkenheil & Co., Genthinerstrasse 19, Berlin, Germany.

fecting of the preparations is that of Messrs. Squire & Sons, 413 Oxford Street, London, W. Their experiments, carried out in December, 1906, and the three following months, were of the utmost value, and upon them was based the demand for the standardization of the preparations which I made in America in March, 1907.

We may still retain the proposition that the complete treatment, where possible, is threefold—hypodermal, oral and local. I will deal with the oral treatment first. This has hitherto been considered the least important, and formerly I have discussed it curtly.

It still is true that the attempt to treat cancer by the oral administration of the pancreatic ferments alone is little better than a farce, *as it is usually made*, though this statement must be modified in the light of Von Leyden's work as regards cancer of the stomach. Trypsin is liable to be destroyed with very great rapidity in the stomach, in accordance with the general principle that even weak solutions of acids rapidly destroy all ferments, with the notable exception of pepsin. In so far, then, as any kind of good is to be expected from the oral administration of this ferment, it must be administered before meals—say an hour before food—at a time when the stomach probably contains no free hydrochloric acid. We may hope that, thus administered, the ferment will pass on into the bowel undestroyed.

Now, everything which makes for the better health and nutrition of the patient is of value. As a rule, there has been great loss of weight, and this has to be recovered whilst absorption of the growth occurs, this absorption in itself tending to interfere with the patient's nutrition. Thus quite apart from any hypothesis as to inactivity of the pancreas in such cases—of which we have no evi-

dence—we may be assured that the oral use of pancreatic extract before meals may aid the digestion, and thus the general nutrition. This is no negligible service, though as such it has no bearing whatever upon the history of the tumor from which the patient is suffering.

Formerly I used to state that the simple administration of the ferments by the mouth could not be expected to have any really remedial action. I argued that there was no positive evidence to show that active trypsin in the bowel, whether formed there from trypsinogen in the natural manner, or reaching it from the mouth, is absorbed into the blood. No doubt such absorption occurs in the empty bowel before birth, when—as has been lately proved again by Barbera—trypsin is formed in it, as after birth; but there was no evidence that after birth such absorption occurred. Thus it seemed most essential not to recognize mouth administration as a serious and effective method. If trypsin had been demonstrated as normally present in the blood, the case would have been different; but, so far from this, the physiologists taught—erroneously, as we now know—that the injection of trypsin into the blood promptly leads to the production of an anti-ferment.

The recent German work has greatly altered our conceptions on this point. Prof. Von Leyden has recovered active trypsin from the urine after its administration by the mouth—conclusive proof of its absorption into the blood from the bowel. (Absorption of anything but water from the stomach scarcely occurs at all.) In the absence of any such supposition as that, in cancer, the bowel is modified in some way so as to interfere with the absorption of trypsin, it therefore follows that the oral administration of trypsin should be a perfectly effect-

ive mode of treatment ; and in point of fact I have word of a case, as yet unreported, in which oral administration alone did prove quite effective. It would seem that, if once the trypsin passes safely through the stomach, where hydrochloric acid is too frequently lying in wait to destroy it, its absorption into the blood should be effected. Now it is absorption into the blood that is the whole object of the hypodermic administration of the ferment, and it matters not at all, of course, whether this absorption occurs from the bowel or from the subcutaneous tissues. It is further to be noted that the risk of gastric destruction of trypsin is less in cancerous than in healthy patients, since the secretion of hydrochloric acid by the stomach is diminished or suspended not merely in cancer of the stomach, as used to be taught, but in cancer generally. In any case this risk can be averted, and it is conceivable that the adequate administration of trypsin by the mouth may prove itself capable of replacing altogether the hypodermic method of administration ; and also that here we may have a simple, convenient, painless method of preventing the development of cancer in persons in whom it is threatened. At present one can only say that, if it be possible to do without hypodermic injection, complicated as it is by so many chemical difficulties and immediate inconveniences, we shall have infinite reason to be grateful. Even now, however, the demonstration of Von Leyden demands, as an immediate practical corollary, that the extensive use of active trypsin by the mouth should always be practiced as a necessary part of the treatment. If, as I suspect, the factor of time is important, as it is in the case of such drugs as sodium salicylate, which is excreted by the kidneys with extreme rapidity, then, as in that case, it is desirable to

administer the remedy at intervals far more frequent than is practicable with hypodermic injection. Certainly if I believed myself to have a cancer, or symptoms suggesting the presence of the disease, I should forthwith put myself upon large doses of trypsin, taken at least three times a day on an empty stomach, whatever other measures I sought to employ. It may be desirable to neutralize the possible (organic, not hydrochloric) acidity of the stomach, which in dyspepsia—such as is common in cancer—may have continuously acid contents, by giving sodium bicarbonate before the trypsin.²

The local treatment is, of course, not applicable in all cases, but those who are acquainted with the general facts of cancer will realize that in the majority of cases it is available, even in cases where no ulceration has occurred. Thus in cancer of the mouth and tongue and lip and cancer of the womb, local applications of the pancreatic ferments are possible. Again I would insist that these cannot be expected to affect the deeper parts of the tumor, which are the parts where extension and invasion of the healthy tissues are chiefly occurring. Nor can local application be expected in any way to interfere with the occurrence of secondary tumors by means of the passage of malignant cells through the lymphatic vessels or the veins. Nevertheless such local treatment in many cases effects the very rapid digestion and disappearance of great quantities of tumor tissue, and does so in a manner infinitely preferable to that only too commonly effected by the growth of microbes upon it. Nothing could have been more remarkable than the results in the first case I

²Certain of the oral preparations are most nauseous and actually upset the digestion—a strange effect of digestive ferments. The glycerine, etc., in such must somehow be dispensed with.

witnessed, now nearly two years ago, which followed the local application of *lotio pancreatis*. Wherever a swab soaked in this preparation was applied the tumor simply melted away. It need hardly be pointed out that it is much better for the patient to have a given quantity of malignant tissue thus disposed of, than to have the products of its digestion absorbed into his blood. Both liquid and solid preparations for local use may be obtained, and I would strongly insist that these should be employed wherever their use is practicable. Though their employment will cure no cancer, except possibly very superficial tumors of the skin, they constitute most valuable aids to the treatment. Let it be observed that the local use of these ferments does not cause pain, that it does not in any way affect normal tissues, and that it is in no way comparable to the use of caustics, such as caustic potash, arsenic and the like. The practitioner may still be troubled for some time to come by signs of local irritation caused by the glycerine and acetic acid contained in certain of the washes sold for local use.

I now pass to the essential part of the treatment, which is the hypodermic or subcutaneous injection of active preparations of the two pancreatic ferments, trypsin and amylopsin. "The amylopsin," says Dr. Beard, "is specially meant to be used in the later periods of treatment, to help to clear away the remains of dead tumor; but from the start it should be given against any bad symptoms, such as nausea, vomiting, pain in the back, drowsiness, high arterial tension, albuminuria, and œdema generally. Bad symptoms, which are not always prominent features, bear resemblances to eclampsia, and are due to the like cause,—products of degenerating trophoblast (tumor). In uterine and abdominal cases in general it is

advisable to give an injection of amylopsin twice weekly from the start." This question is further discussed in another chapter.

The hypodermic injections may be made anywhere, but *not* into the tumor mass—as made by Prof. Von Leyden—where they are apt to cause considerable swelling and pain. Dr. Beard has made this recommendation from the very first, and, indeed, in the preparation of this whole chapter I am greatly indebted to the general directions for treatment which, since the early part of 1906, he has freely sent to every physician who has written to him.

The injections must not be made into muscular tissue, where the injections hitherto supplied are liable to cause much pain, nor, if possible, should they be made immediately under the skin, and for the same reason. If possible they should be made into the fatty subcutaneous tissue, though this is only too frequently wasted in patients suffering from cancer. The arm, especially the upper arm, and the buttock, are the sites most frequently chosen. The neighborhood of the backbone must be avoided. For reasons undivulged, the Middlesex Hospital observers chose the tender skin of the abdomen—with the disastrous results which they record.

The skin at the site of injection must be scrupulously cleansed and sterilized. A little eucaine or other local antiseptic may be employed in order to lessen the pain of the injection in the case of nervous or sensitive patients. The greater part of the discomfort, however, so far as I have observed, is due not so much to the piercing of the skin by the injection-needle, as to its distention when the fluid is forced under it. This is

another reason why injection into the loose subcutaneous tissue is preferable.

So far as has been at present observed, there is a marked difference between the painfulness of the two injections. The amylopsin causes very little local trouble indeed, if any. The trypsin, however, is apt in many patients, to give rise to some swelling, local discomfort and pain. This depends not at all upon any inherent difference in the relations of the two ferments to normal tissues, but merely upon the different mode of preparation which is employed in the two cases. A firm lump may sometimes form at the site of injection, which will not disappear for some days. It has been suggested that eucaine should be injected immediately after the ferments, but it is doubtful whether this is necessary, and the further question has to be asked whether eucaine has any adverse influence upon the ferments. The best, simplest, and most effective procedure is to use ice. When the injections are made into the arm, pieces of ice may conveniently be bound upon it and kept there for even so long as two or three hours, being renewed if necessary. This gives the greatest relief and comfort in every instance, and until injections which cause no pain can be prepared, the use of ice should be employed as a routine procedure. Lately it has been my experience that the ice is no longer necessary.

The syringe is best made entirely of glass, and must be rigorously sterilized. For this purpose heat is often employed. If, however, the syringe be boiled, it must be cooled before the injection is sucked into it. On no account whatever must the injection be exposed to heat, which will rapidly destroy the trypsin and render the whole proceeding futile. I have seen perfect success fol-

low the sterilization of the syringe by means of the successive employment of perchloride of mercury (1 in 1,000), boracic acid, and sterilized distilled water. This is not so troublesome as it sounds, and avoids any risk that impatience may lead to the use of the syringe when it is too hot.

Some of the injections still upon the market require dilution. This is a defect, because it leads to risk of two kinds in the hands of careless practitioners. The water used for dilution may be insufficiently cool, or may be imperfectly sterilized. The water to be used must be sterile, cool, and distilled. If it be sterilized by boiling, on no account whatever must its cooling be hastened by adding the cold injection to it. One might as well omit to add the injection altogether as destroy it by heat in this fashion.

Says Dr. Beard: "*The greatest care and cleanliness should obtain, and the dose should be graduated with careful regard to the reactions observed.* The course of the treatment should be: *Injectio trypsini*, full doses up to two ampoules daily for four weeks; then *Injectio trypsini* and *Injectio amylopsini* alternately on different days for ten to twelve weeks *and longer* in the same way, and in doses of one to two ampoules; and, finally, *Injectio amylopsini* alone daily, or every other day, for four weeks, *and longer*, in doses of one to two ampoules.

"N.B.—It is impossible at present to state any exact period for giving the alternate injections of trypsin and amylopsin. The time will vary in different cases, but the use of trypsin should not willingly be stopped entirely, for although the main mass of a tumor may appear to be dead, there may still be a few living cells within. Moreover, the possible existence of metastases should not be

overlooked. *The physician must be certain the tumor is all dead before he relies on injections of amylopsin alone.*"

To this Dr. Beard now adds: "With very many post-operative recurrent cases no amount of dose will have any effect in stopping the tumor from 'running its parabola.' Success may come, but it cannot be anticipated with certainty in post-operative recurrent cases. The treatment, as a scientific one, is not really intended for such cases, for it is not scientific to operate upon living cancer or asexual generation." (I believe, myself, that this decidedly understates the power of the treatment, even in post-operative cases.) "The 'X' rays should not be used along with this treatment. The period of stoppage of the injection of amylopsin will also vary in different cases. Where much dead tumor remains, it may, and should, be given indefinitely, as long as any remains persist, in daily doses, or every other day, *and its use should not be willingly given up.* If for any reason it be dropped, a careful watch must be set upon the patient, and on the appearance of headaches, drowsiness, loss of appetite, nausea or vomiting, or other bad symptoms, its use must at once be resumed, in doses and at intervals in the discretion of the physician. In malignant sarcoma much more vigorous treatment may be needed, at any rate for a time, until the tumor be killed (not after), for I have known as many as sixty ampoules, injected two daily, to produce no effects on a sarcoma."

This whole question of dosage is a most important and difficult one. The doses employed during the first year of the treatment were always believed and maintained, both by Dr. Beard and myself, to be utterly inadequate, quite apart from any question as to their not being what they purported to be. It is, of course, relatively easy for

the non-practitioner, who is not directly responsible for any patient, to make this criticism. The vast majority of those who have used the treatment, even where they have employed active preparations, and employed them properly, have used ridiculously inadequate doses. This has by no means been entirely their fault. The earlier preparations put upon the market were such that adequate doses of them would have been so bulky as to be almost impracticable. The case is very different now. Apart from this, however, many have had a superstitious fear of the ferments, and have gone on using doses which no one could well expect to be effective, even though no symptoms of any kind were obtained. The so-called 2 per cent. strength of trypsin, for instance, which one practitioner recommends, is ludicrously inadequate. "Till we know more of this toxic agent, it should be used with care," says Dr. Shaw Mackenzie; and it is this entirely false conception of trypsin which has disastrously interfered with the success of the treatment, by leading practitioners to employ doses of homœopathic tenuity, and then declare that no result is, or can be, obtained.

We must cease entirely to use any unit of dosage other than units of digestive capacity. We can go neither by number of drops nor by asserted percentages of the ferments. Questions of dosage must be discussed in terms precisely similar to those employed in the case of the treatment of diphtheria by the anti-toxin. It seems probable, then, that a safe and effective dose is one containing five hundred units (Roberts) of tryptic activity and two hundred of amylolytic activity: most certainly not less. This proportion between the two ferments seems to be the most useful one. Injections of pure trypsin (free from amylopsin) should never be employed at all. Such

injections are not obtainable, and I hope the manufacturers will not attempt to produce them. Such a dose as I have named is contained in one cubic centimeter—that is to say, about seventeen drops—of Messrs. Squire's preparation, which they call Standard II. This requires no dilution, and its bulk is relatively so small that it cannot be expected to cause much local disturbance. As for the amylopsin, a dose of two hundred units, comprised in the same bulk, seems to be a satisfactory one.

As to the time periods named by Dr. Beard above, they can only be regarded as giving some indication for early cases. In the advanced cases which have exclusively come under this treatment hitherto, much more prolonged administration has been necessary. On the other hand, much shorter administration has sufficed for the destruction of a small nodule—even though recurrent—such as that reported by Prof. W. J. Morton in the *New York Medical Journal*, March 9, 1907.

I quote further from Dr. Beard: "The question of proper dosage is not yet decided finally, and it will probably be found to vary with the different cancers. In the foregoing I have preferred to err on the safe side (in advising sufficient for an ordinary cancer, *not a sarcoma*). In some cases, and in small epitheliomata, no doubt less would suffice. While the tumor is alive, and for some little time after, it may be taken that the cancer-ferment, *malignin*, and the pancreatic ferments, especially *trypsin*, act toward each other somewhat like *toxin* and *anti-toxin*. The killing of the cancer-cells of any ordinary unoperated cancer, if not large, is not at all difficult. Indeed, it may be brought to pass in less than a month. The real difficulty, then, arises in the removal of the remains of the dead tumor. If this be left to treatment, and be not

done surgically, it may be a matter of many months, during which the use of trypsin and amylopsin (injections) must be kept in view at all times. In a successful Italian case of inoperable cancer of the tongue (of three years' standing), it may be taken that full treatment began at the end of February, 1906, stopped about the middle of June, 1906, but the final remains of the tumor only took their departure at the end of September, 1906. Attention should be paid to a good, liberal, nourishing diet, with plenty of water and milk to drink. For a few weeks at the start salts and acids should be avoided.

"Signs of improvement usually appear after some ten injections.³ They are: cessation of pain, increase of strength, improved appearance, loss of discharge (if any), unless the tumor be sloughing away, loss of smell (if any), and soon marked shrinking and softening of the tumor-mass. The treatment should not be dropped for a time, for there is danger, especially in the first three months, of the formation of poisonous substances from the degenerating tumor."

It is necessary to insist again upon the entirely tentative and provisional character of this whole chapter. If our critics and those who have failed had carefully published their experiences, or anything fairly to be called criticism (*i.e.* judgment), we should doubtless know much more now. But this innovation has not received from the conservative that enlightening criticism which is at all times the humble but necessary function of conservatism. The central question of dosage remains quite undetermined, and will so remain until nothing but standardized preparations, used within a standardized time limit, are employed. In the case of recurrent sarcoma

³Much sooner with the best injections in my recent experience.

to which Dr. Beard refers, for instance, no one can say how much active trypsin was actually employed. Far smaller "doses" have brought a recurrent sarcoma under control and destroyed it, as in Dr. Doran's case (noted later). But these doses may actually have been far larger than those in the case of failure.

Nevertheless, it is impossible to exclude the exceedingly probable supposition that ultimately the necessary dosage—actual, not nominal—will be found to vary with different types of growth. Elsewhere I discuss such *a priori* data as we at present possess in this relation; *a posteriori* data there are as yet substantially none.

I do not doubt that the questions of abscess formation, and of destruction of the ferments by heat at any stage, are subsidiary as causes of failure, compared with inadequacy of dosage due to other causes. Absolutely ridiculous percentages—and these only nominal—have been employed. Such preparations should not be even obtainable; for any fraction of any preparation can be used if desired. Similarly, inadequate doses even of adequate preparations have been used. It is incomprehensible how practitioners, having nothing else in the world to offer their patients, have given the new treatment the sort of perfunctory and farcical trials to which at least two great hospitals in London have publicly confessed. If results are not obtained at first, and neither constitutional symptoms nor results show in the growth itself, the dose must be rapidly increased. In any case, the practitioner does not know what doses he is really giving, unless he employs a standardized injection made the same day. He is accustomed, of course, to employ that poison-therapeutics which has held sway in medicine for so many ages and is now doomed; and his experience with

the poisons of his daily employment teaches him to beware of an overdose, and to believe in an upper limit of safety for everything he uses. Trypsin proves by its origin in each of us that it is *not a poison*: the German workers have proved that enormous doses cause no symptoms in the lower animals (free from cancer), even when injected into the blood: if and when the injection causes constitutional symptoms these coincide with, as they depend upon, favorable changes in the tumor: and these symptoms can be controlled by amylopsin. When no results of any kind appear, either the disease is not cancer at all, but an innocent tumor, an inflammatory swelling or what not; or else the injection is inert; or else the growth may be of a type so malignant—whether from the first or as the result of operation—that its ferment cannot be mastered by trypsin; or else the dosage is too small. Having no other recourse in the world, the practitioner is surely bound to investigate the activity of his preparations, and, if no symptoms result, to increase the dose rapidly. There is no toxic, still less a lethal, dose of trypsin *as such*, though there may be doses indirectly toxic to cancer patients. In the absence of toxic symptoms (which are not due, and cannot possibly be due, to its direct action, but are the index of its desired activity), the dose must be increased. Any one with any experience of the treatment will recognize at once that the failure of the Middlesex Hospital observers—which has so potently swayed opinion in Great Britain, and which one or two enemies of trypsin, seeking to bolster up their early statements, have exploited and more than exploited in America—was in all probability due partly to the smallness of the doses employed. Nominally the doses were evidently far too small: actually doubtless far smaller.

But an experienced observer, uninformed as to the doses employed, and the surgical histories of the cases—which last are not stated—would at once condemn them as inadequate from the mere fact of the absence of constitutional and local reaction (in the tumor. There was most abundant local reaction at the site of injection.) This instance shows the importance of avoiding assumptions of futility when testing a treatment. If the observer is not a skeptic he attributes failure possibly to himself, and modifies his method. If he is a skeptic—or, rather, an active disbeliever—he attributes his failure to the inherent futility which he began by assuming, and makes no attempt to modify his method. This would not be the behavior of the true skeptic, of course, in the literal and proper sense of that much abused word. He would “look about,” which is the meaning of the word. The Middlesex experiments—I do not refer to the earliest ones, which were a mere burlesque—were undertaken as a direct consequence of my articles in the *Pall Mall Gazette* last December, and I should have been delighted, of course, to observe them, and offer any help I could; but neither Dr. Beard nor I was even informed of their occurrence.

In concluding a chapter which I repeatedly describe as provisional, I would ask for what must be of the greatest value—the help of the veterinary surgeon. Nothing has yet been made of the opportunities furnished by cancer in the lower animals, apart from the mouse. In them it is perfectly legitimate, for instance, to experiment with the treatment, even in very early cases which the surgeon could remove *in toto* with practical certainty. It is by this means, I believe, that we shall learn in a very short time, and without risk to any human being, what could

scarcely be learned at all on that condition from human patients. The young veterinary surgeon has a splendid opportunity in this field at the present time. He can inform us as to the practical limits of dosage of the ferments; the length of time during which one dose acts, judged by the rate of excretion; the proper variations of dosage, with (1) the type of the tumor, and (2) the factor of its mere mass; and he can discover for us the ideal proportion between trypsin and amylopsin in any dose. This may be a constant proportion, but the point seems not quite certain to me. The amount of digestion that may be effected by a given quantity of a ferment is not finite—a fact we are apt to forget. A single dose, a single molecule, of trypsin, is capable of digesting an infinite quantity of any proteid that it can digest at all; and thus a single dose of trypsin might conceivably digest an entire tumor, however large, if it digested any portion of it, provided that it was not removed from the tumor by the circulation or destroyed by the cancer-ferment or ferments. Only these possibilities necessitate the repetition of a dose itself effective at all. I shall be deeply interested to learn the exact facts of the excretion of a dose of trypsin. Von Leyden, Bergell, Pinkus, Pinkuss, and others, have shown that the ferment can be recovered in the urine in an active state; but can it *all* be recovered (1) in health, (2) in cases of cancer, (3) equally in cases which it markedly affects and those which it does not appear to affect at all? Is it destroyed, so as to be irrecoverable, in these cases, assuming them to exist? How soon does it appear in the urine, and at what period does it disappear from the urine? These are only a few of the questions which will occur to any pharmacologically-minded reader, and they are one and all of practical

moment. I believe they will be most rapidly answered by the veterinary surgeons, and I earnestly commend the inquiry to them. Dr. Beard has found the road, and it is for others to march to the utter conquest of cancer.

In the next chapter I discuss the important work of Dr. Cleaves in this relation. Here I briefly add the speculation, elsewhere referred to, that the beginning with small and gradually increased doses rather suggests the likeliest fashion *in which to immunize the tumor*, and also the observation that all ferment actions are reversible in certain conditions, and that this fact has yet to be studied in the present connection.

This is perhaps as convenient a place as any in which to discuss an important paper by Dr. Monckton Copeman, F.R.S., which appeared in the *Practitioner*, August, 1907. As a preliminary, one remarkable sentence of the author's may be quoted. He says that the new treatment "has apparently been proved incapable, alone, of preventing the inevitably fatal termination of the disease." This extraordinary phrase, "proved incapable," beggars my capacity for comment. I have no available words to use when a distinguished Fellow of the Royal Society, who is surely acquainted with the meaning of the word proof in exact thought, and with the nature of scientific proof, can declare that the treatment has been "proved incapable." What would Dr. Copeman and every one else say, I wonder, if I had adduced as proof for the treatment evidence of the quality which he regards as apparent proof against it? Seemingly it is necessary to observe once more that a negative result—assumed for the argument to be validly obtained—demonstrates nothing beyond itself, while a positive result—similarly assumed to be validly obtained—proves in the proper sense. Each

alike requires confirmation. But there is no comparison between the weight of the two, otherwise the blind man is entitled to assert as proved that the sun cannot be seen—he cannot see it; the fact of his observation, or failure of observation, is valid, but it proves nothing against the man who can see. These are the very *elementa* of logic.

Dr. Copeman does, however, admit some results from the treatment, including relief from pain, which I note, because it is incapable of inclusion—though he does not note the point—within the very interesting explanation which he furnishes. Brushing aside the old methods of approaching the problem from the side of microscopic appearance, Dr. Copeman makes a fresh start from the chemical standpoint, and this it is which makes his paper so welcome. He returns to the conception, which had been thought disproved, that cancer is, in a true sense, a constitutional disease—in other words, that the “general body metabolism is primarily at fault.” The evidence of this he finds in the observation communicated by Prof. Benjamin Moore to the Royal Society, March 16, 1905, and noted elsewhere, that in cancer generally, and not only in cancer of the stomach, the secretion of hydrochloric acid by the glands of the stomach is greatly diminished or abolished,⁴ and in the further observation that the blood is usually of excessive alkalinity in cancer. This fact he regards as the first of a series dependent upon it, though the question of its causation is not considered. The blood being more alkaline—or being deficient in hydrogenions, to use the modern phraseology—the gastric glands are unable to produce hydrochloric acid. Now, in the absence of this acid from the fluid or

⁴But, puzzlingly enough, Dr. Copeman finds the gastric HCl *increased* in “cancer-mice.”

semi-fluid material that passes from the stomach into the bowel, there is not produced by the bowel the *secretin* of Prof. Starling, which is normally called forth by the acid stimulus, and which, after absorption, reaches the pancreas and causes it to pour forth its trypsinogen, which, on reaching the bowel, is fermented by enterokinase, with the formation of trypsin. Thus the cancer-patient lacks his pancreatic secretion—not because his pancreas is disordered, but because, in the first place, his blood is too alkaline. Dr. Copeman suggests that the nutritional disturbance of the disease is due, in part, at any rate, to this defect of the pancreatic secretion; and thus he seeks to explain the beneficial results which, as he admits, do in some cases follow the pancreatic treatment. As I have noted, however, this explanation does not cover the relief of pain which Dr. Copeman himself admits; and I am very sure that if Dr. Copeman had himself made observation of this treatment—an opportunity which our critics, almost without exception, have rigorously denied themselves—he would realize that an explanation which does not cover the amazing, immediate, consistent and continuous relief of pain in these cases, is very far from adequate. Dr. Copeman, however, does not admit or consider the possibility that the pancreatic secretion has any specific action upon cancer, and he makes no allusion whatever to the authoritative German work which has exhaustively proved the existence of this specific action. It is a great pity that really responsible and distinguished students should deliver themselves of opinions on the treatment without having observed it for themselves. If I had had nothing but hearsay to base my crusade upon, I should have been rightly condemned

by every one; but the opponent who has nothing but hearsay to go upon is not criticized on that ground by any one. For the advocates of the treatment, the most rigorous critical criteria; for its opponents, none whatever—not even the expectation that they shall publish their experiments! I must return, however, from what is surely a warrantable digression.

Dr. Copeman admits, then, that the pancreatic treatment may be of some value, but his explanation is not that trypsin is thereby introduced into the blood—for he apparently does not contemplate at all the possibility that the trypsin formed in the bowel from the pancreatic secretion may normally enter the blood—but that the treatment stimulates the pancreas to pour forth its secretion into the bowel, and possibly also to pass into the blood some “internal secretion.” Evidently Dr. Copeman is not so far from what I believe to be the right conception, if he can suggest that the pancreatic treatment may be of value in causing the patient’s pancreas to pour forth some internal secretion into the blood, even though he presumably supposes this to affect the general nutrition only.

It might have been expected that Dr. Copeman would now proceed to recommend the adoption of the pancreatic treatment as a palliative agent in dealing with cancer. But, curiously enough, he proposes to effect the end which the pancreatic treatment directly attains by the very indirect method of *administering acids*, in order that the alkalinity of the blood may be lessened, the secretion of gastric acid increased, secretin formed, and the pancreas, finally, stimulated. He tells us that, at the time of writing, he is making trial of Prof. Metchnikoff’s

lactic acid milk for this purpose. It will be interesting to hear what results he obtains.⁵

Meanwhile, however, it is necessary to look further at Dr. Copeman's argument. "Cancer constitutes," he says, "the local manifestation of perverted body metabolism"—the evidence of this being the defective secretion of hydrochloric acid, dependent upon the increased alkalinity of the blood. Without present reference to the question whether, at least, *some local factor* is also necessary—cancer being, as I now believe, neither a constitutional disease only, nor a local disease only, but necessarily both—let us address ourselves to this question of the increased alkalinity of the blood, the causation of which Dr. Copeman does not consider. We have to remember that, in this continuous universe, to find a cause is only to raise a fresh question as to the cause of that cause. Now, if increased alkalinity of the blood be the fact of "perverted body metabolism" of which "cancer constitutes the local manifestation," and if the arrest of pancreatic action be the consequence of that change, surely it is suggested that this arrest of pancreatic action is the factor that permits or determines the "local manifestation." In a word, surely Dr. Copeman's own reasoning leads to the conclusion that the pancreatic secretion, internal or external, can prevent the growth of cancer. Again it appears to me that Dr. Copeman's own words and arguments do, in effect, entitle us to claim him as almost the first distinguished convert in this country to Dr. Beard's theory that trypsin must control cancer—even though, in-

⁵Citric, acetic and other organic acids are oxidized in the blood with the formation of carbonates and *increased* alkalinity. I suspect that this may happen with lactic acid. Also lactic acid destroys trypsin, even in greater dilution than hydrochloric acid!

stead of giving the pancreatic secretion directly, he prefers to evoke it by giving lactic acid bacilli—a therapeutic method perhaps the most indirect ever suggested, involving as it does the (dubious) interposition of some half-dozen delicate bio-chemical processes. It may be noted, also, that it is scarcely necessary to attribute to pancreatic injections—still less to lactic acid milk—as against pancreatic injections, any virtue as regards stimulating the pancreas to produce its internal secretion, since this internal secretion must in any case be present in the injections, made as they are from the fresh pancreas-gland. The more Dr. Copeman's arguments are examined, the more support they render our case, though he makes no mention of Dr. Beard or his teaching, and includes the usual gibe at the treatment as being much vaunted in the lay press. Were it not for this said lay press, we should still be as we were at the end of the year 1905, so far as cancer is concerned, and many persons now above ground would be beneath it.

Now it is necessary to inquire into possible variations in the alkalinity of the blood at different ages, and into the possibility that this alkalinity is excessive prior to the development of cancer. The facts, I submit, entirely negative Dr. Copeman's theory. If the excessive alkalinity of the blood were primary, or proximately primary, as he suggests, defective secretion of hydrochloric acid, and, in consequence, marked and unmistakable dyspepsia, should be the constant or common precursor of malignant disease. This is certainly not so, and the fact is conclusive in my opinion against Dr. Copeman's hypothesis.

On the contrary, I believe that the increased alkalinity of the blood in malignant disease *follows upon*, and is not a cause of, its development. I believe further, as against

Dr. Copeman, that this increased alkalinity, so far from being a sign of perverted body metabolism, of which the disease is the local manifestation, is a compensatory and protective mechanism on the part of the body. Trypsin acts best in an alkaline medium, as is generally known; the cancer-ferments act in an acid medium, and the digestive processes by which a cancer lives are acid. I need not here revert to this question. But the therapeutic indication, I believe, so far from being the administration of acids, is the administration of alkalies, which will tend to favor the activity of trypsin and to disfavor the activity of the cancer or trophoblastic ferment or ferments. I recommended the use of alkalies as an aid to trypsin in one of my early articles "in the lay press"—the only press open to me or to Dr. Beard in *Great Britain* since January, 1906—and I am now more strongly of opinion than ever that this measure is to be recommended as a rational addition to the treatment in some, if not all, cases.

Meanwhile it is desirable that the alkalinity of the blood be examined in cases of spontaneous cure, and I will venture to predict that in these cases—which offer priceless and hitherto wholly neglected opportunities for the study of the disease on chemical (*i.e.* the only profitable) lines—the alkalinity of the blood will be found even higher, if anything, than in cases which are running the usual course.

It may be noted that observations subsequent to those of Prof. Moore seem to show that the diminution or absence of gastric hydrochloric acid in cases of cancer is highly variable and inconstant. These variations may be of great importance, and may be found to correspond with variations in the progress of the disease in the fashion already indicated.

CHAPTER XIV

THE GENERAL ACTION OF THE FERMENTS

PERHAPS there is no other indication of the hopelessness with which the treatment of cancer was regarded, and the dominance of the idea that this is "a surgical disease," than the fact that, notwithstanding the prominence lately accorded to what is called organo-therapeutics, or opo-therapy, and the magnificent success won by it in certain quarters, it actually occurred to no one, so far as I know, to essay the treatment of cancer by such means. The success of the thyroid-gland as a true, specific cure for cretinism and myxoedema, as the latest great achievement of medicine, and the maxim of the curative power of nature as perhaps its most ancient doctrine, together with the fact of occasional spontaneous cure, so vastly significant and so wholly neglected even by the merest speculators—these might surely have led to the employment of some form of organo-therapeutics in cancer long ago, or at least in the closing years of the nineteenth century. This, however, as a passing reflection, sufficient to show how repeated failure had checked fertility of suggestion, and how entirely the surgeon, practicing in modern guise the oldest and rudest of all healing measures, dominated the situation.

Now, though the pancreatic ferments are normal inhabitants of the body, and, therefore, not drugs in the ordinary sense of the word, but rather special foods, it

is necessary to study their consequences when administered in health, which belong to pharmacology, and when administered in malignant disease, these last belonging to clinical therapeutics. This whole subject is still in its infancy, but certain myths have already been dissipated, and facts observed, especially by Dr. Margaret Cleaves, in New York, and by Drs. Pinkuss and Pinkus in Berlin. Detailed reference is made elsewhere to the results of these latter workers, and here I will refer especially to the careful and laborious and prolonged observations of Dr. Cleaves.

As a preamble, we may mention, merely in order to dismiss it, the notion, elsewhere referred to, that trypsin entering the blood would digest the body. That, of course, is as untrue as any belief can be.

But apart from this, our beliefs as to the pharmacology of trypsin, hitherto, were simply that, administered by the mouth, it might facilitate the process of digestion, assuming that it escaped destruction by the hydrochloric acid of the stomach; and secondly, that, injected into the blood, it aroused the formation of an opposing substance to which the name of anti-trypsin was given. This last belief has been disproved by the German workers, who have, however, found an anti-body when extracts of decomposing pancreas are used.

But what will be the action upon the normal body of large doses of active trypsin injected into the blood? Until the rise of the new treatment it should have occurred to no one to expect poisonous symptoms, for it should have occurred to no one to regard this normal constituent of the body as a poison: we have seen, however, the old delusion as to its digesting the body. But the demonstration of its poisonous action upon cancer, and the excite-

ment of toxic symptoms by its use in cancer, led to the confirmation of the opinion in many quarters that the ferment is essentially a poison, to be regarded as such, used with the utmost caution, and especially with scrupulous reference, as in the case of other poisons, to an upper limit of safety in its dosage. Now, before we accept or dismiss this conception, it is absolutely necessary to study the pure pharmacology of the drug—its action upon the healthy body. It was the non-existence of pharmacology, and the observance of effects produced in disease alone, that for ages prevented the evolution of a scientific therapeutics. If we do not know the action of a drug in health we cannot really know its action in disease.

Reference has elsewhere been made to the first experiments of Pinkus, who showed that relatively gigantic doses of trypsin, injected under the skin of a healthy dog, produced absolutely no symptoms or results whatever, except an increase in weight, which might well be attributed to the facilitation of the animal's digestion. These experiments were of much importance, for the simple reason that nothing as to the action of trypsin in the blood can be properly inferred from the administration of the drug by the mouth, which, unless exceptional precautions are taken, must involve its almost immediate destruction by the healthy stomach. The experiments of Pinkus were also important as proving that trypsin can circulate in the blood as such, and be removed from it by the kidneys, without suffering change.

A whole series of important questions are thus raised, and definite inquiry must be directed to their solution. Pinkuss and Pinkus have proved for animals in health, and they and Von Leyden for cancerous human patients, that trypsin may circulate in the blood and be excreted

by the kidneys. Von Leyden gave the trypsin by the mouth, and it must have been absorbed from the bowel. But if trypsin, given by the mouth, can be absorbed from the bowel of cancerous patients, trypsin formed in the bowel can be similarly absorbed by healthy or non-cancerous persons. Bier has proved the existence of a proteolytic ferment (or ferments) in the blood of the normal lamb and pig—especially the latter, the pancreas of which is highly active. It is, therefore, urgently necessary to inquire into the presence of trypsin in normal blood, and, if it can be identified there, its variations at different ages and in cancerous patients to whom trypsin is not being administered. But the knowledge already in our possession shows that the kidneys, by means of their secretion, furnish an index on this point. It is necessary, then, that the urine be examined for trypsin, not merely in animals or human beings, healthy or cancerous, to whom trypsin has been administered, but in animals and human beings, both in health and in cases of malignant disease, to whom trypsin has not been administered. Many questions readily suggest themselves. Is trypsin normally to be found in the urine—*i.e.*, normally present in the blood—of healthy persons? Does it tend to diminish at the ages specially liable to the incidence of cancer? Is it diminished in, or absent from, the urine of cancerous patients? It seems to me that the answer to these questions may prove to be of enormous importance, and they should be easily and quickly answered by modern methods of investigation. Here we may be on the verge of the elucidation of the conditions which permit the growth of cancer in one patient and not in another; at one age and not at another; and it may appear that the absence of trypsin (or some other cancrotoxic ferment) from the

urine—in which, as we can scarcely doubt, after studying the work of Bier, it *should* be normally present—may constitute a warning of the imminence of cancer, and an obvious prophylactic indication.

An important point must be made here. Though I most heartily welcomed, and have ever since given prominence to, the demonstration of the excretion of trypsin by the kidneys, after either hypodermic (Pinkus) or oral (Von Leyden) administration, since it suffices to prove that these methods will insure its reaching a malignant growth, injection into the growth (and all secondary growths) being thus unnecessary—yet, apart from its proof of this possibility, the fact is much to be regretted. Evidently, it would be much more desirable that the precious remedy be not so removed, but permitted to circulate in the blood for prolonged periods. Far more satisfactory would it be if, like many drugs, trypsin had a “cumulative” action, the proportion of it in the blood gradually mounting as the treatment continued. If this were so, obviously the whole character and duration of the treatment in practice would be modified. Much work will have to be done in this field. At present we have the work of the German observers alone to guide us. I am anxious to know, for instance, why Drs. Pinkuss and Pinkus should find trypsin in the urine, in certain cases, so late as after the forty-eighth injection, *for the first time*. Was this an indication of saturation of the blood by the ferment? Many allied questions might be asked, and will, ere long, be answered.

Systematic experiment is still lacking as to the effect of the administration of trypsin by the skin in healthy human beings. There is every reason to suppose that the results would be similar to those obtained in the dog. Trypsin is not a poison to normal tissues, and can have

no poisonous action upon a body which contains only somatic tissue—that is to say, tissue proper to the body itself. According to the theory of Dr. Beard, trypsin is “the architect of the soma”—that is to say, of the body. It is by tryptic digestion of food material that that food-material is built up into the body, and it is inconceivable, therefore, that trypsin can have any action during life upon the soma or sexual individual, “while its action is direct and utterly ruinous upon trophoblast or asexual generation.”

At this point some precise experimental help is afforded us in a very valuable and original paper by Dr. Margaret Cleaves.¹

In this paper, Dr. Cleaves quotes an illustrative case where a patient was treated by her with the pancreatic ferments, on the mistaken diagnosis by the microscope, that the patient was suffering from cancer. She says that the results obtained were similar to those obtained by Dr. Pinkus in his experiments upon healthy dogs. I quote: “This patient was given injections of trypsin of special strength daily for four weeks; in the first week, from one-third to one-half ampoule, and afterward from one to two ampoules, without any amylopsin, without any reaction, and with steady nutritive gain. This was evidenced by the urine analysis as well as by the patient’s appearance and condition of improved metabolism, and her gain in weight from December 2, 1906, to February 15, 1907, of twenty pounds. She never had a rise of temperature, nor any save local reaction from the punctures.” This case supports Dr. Cleaves’s opinion that

¹“The Physiological Action of the Pancreatic Enzymes, with special reference to Hematology, Urinology, and Clinical Pathology.” *N. Y. Medical Record*, June 1, 1907.

“in non-malignant conditions, large and long-continued doses are well borne, as there is no reaction other than the local one at the site of the injection.”

This proposition is of immense importance, not merely because it affords a correct conception of trypsin, teaching us that, if it be a poison at all, it is only a poison to cancer and normal trophoblast, but more especially because it teaches us to interpret correctly such toxic symptoms as may arise in the course of treating patients. We have to learn, first of all, that these are not symptoms of poisoning by trypsin, there being none such; but rather the occurrence of these symptoms, in the first place, constitutes a confirmation of the diagnosis of malignant disease, and, in the second place, depends upon, and therefore demonstrates, an action of the ferment upon the malignant tissue. Thus in cases where no toxic symptoms are observed, not even to the extent of an occasional rise in temperature of one or two degrees, the strong presumption is—assuming malignant disease to be present—that inert, or practically inert, injections are being employed. I speak now of the use of trypsin together with the small quantity of amylopsin that accompanies it, as the use of sufficient amylopsin controls these toxic symptoms.

But we must now pass to consider the question which is evidently raised by the foregoing. Clearly understanding that the pharmacological action of trypsin is *nil*, we must inquire into the general results of its administration when there is present the malignant or trophoblastic tissue upon which alone it can act. This is a matter of the utmost importance on account of its relation to the question of dosage. We may begin by discussing the local reaction.

This local reaction, which has not infrequently been a real obstacle to treatment, has nothing whatever to do with trypsin as such, any more than had the abscesses which were produced by the first American reporter on this subject, and, on at least one occasion, by the Middlesex Hospital experimenters. Local symptoms have depended upon the introduction of living micro-organisms, upon the presence of acetic acid in the injections, or of glycerine or other irritant substances used for purposes of extraction or preservation of the ferment. Dr. Luther reported, as long ago as February, 1907, that he had made five hundred injections without an abscess; and Dr. Meggitt, in the first report of real value that appeared in Great Britain (*General Practitioner*, August 31, 1907), observed that he had made nearly one thousand injections without any such result. The latest and best injections, of which I have been watching the results for nearly a year, cause scarcely any local reaction whatever. The previous experience, however, has been that there is a marked difference between the injections of trypsin and amylopsin, in this respect, and the suggestion has naturally been that this is due to a special action of the trypsin. The manufacturing chemists do not inform us as to the details of their various methods, but there is no question that some irritant agent or agents are, in most cases, employed in making the trypsin injections, which are absent from those of the amylolytic ferment.

Of far greater moment is the general reaction to the use of these ferments in patients suffering from malignant disease. Dr. Cleaves has had very careful examinations made of the blood in her cases, and in all except the patient whose case was wrongly diagnosed as malignant, and in whom she was led by the absence of the

reaction to have the microscopic verdict corrected, she has observed a characteristic change in the blood which leads her to speak of the *trypto-glycogenic* reaction in these cases. It is earnestly to be hoped that her observations may soon be confirmed. She finds, in all her (malignant) cases treated by the pancreatic ferments, a "distinct and very characteristic" increase in the proportion of so-called eosinophile leucocytes, or white cells in the blood. These particular leucocytes are so named since, on staining with eosin, a red dye, they display large numbers of red-stained granules. The percentage of these cells, she finds, rises rapidly, under the treatment, from 1 to 3 per cent. to as high as 25 to 27 per cent. of all the white cells. Now, there is evidence which suggests (see Habershon, *Journal of Pathology and Bacteriology*, December, 1906) that the eosinophile granules consist of the carbohydrate body glycogen, or animal starch. Eosinophilia, as this condition of the blood is called, is commonly observed in various diseases in which glycogen is present in abnormal quantities. Now, malignant tumors are commonly very rich in glycogen—"fully 80 per cent. of tumors in their final stages are associated with glycogen in pathological quantities," and, according to Lubarsch, "glycogen is constant in horny degeneration of a squamous cancer."

In the light of these facts, Dr. Cleaves suggests that "the eosinophile reaction of trypsin is due to a degeneration of cancerous growth," trypsin being the ferment or catalytic agent which splits off glycogen from what Von Leyden and Bergell call the "native albumin" of cancer. Hence Dr. Cleaves says:—

"From these observations, a hypothesis may be formulated, namely, that trypsin acts on intra-cellular matter of

a definite configuration, following the selective law of enzymes, and that the result is a pathological quantity of glycogen throughout the body, manifested especially in the eosin granules, and, to a certain extent, probably stored up in the muscles. As glycogen is not stored up in dead cells, but rather split off from them, and as it is associated in nearly all cases with accumulations in the leucocytes and muscle-cells, it would seem fair to imagine that in cases of trypsin reaction the body is saturated with glycogen."

Dr. Cleaves considers that an important factor in determining the dosage of trypsin is "the condition of the kidneys before and after treatment is instituted." I quote her opinion on this point:—

"Trypsin and amylopsin are excreted mainly by the kidneys, producing a nephritis more or less extensive. Granular casts appear in the urine almost immediately after the first doses of the ferments. The nephritis does not seem to be progressive, the casts and albumin remaining pretty constant unless the dosage is increased. . . . In every instance, casts have appeared in the following order: (1) Occasional fine granular, then coarsely granular, (2) hyaline, (3) epithelial. Under the regimen which forms a part of the supplementary treatment and hygiene of these cases, this nephritis is kept pretty well under control."

It has to be remembered that even the best injections must be of highly complex composition. I am at present far from convinced that this nephritis, even though it be not of a serious character, is, or will always be, a necessary accompaniment of the treatment.

CHAPTER XV

THE GERMAN WORK

THE reader will readily understand that in my attempt to gain a fair hearing through all kinds of noise for what I believe to be the first achievement ever made in the rational treatment of cancer, I long desired the support of some great and universally recognized authority, speaking from some official position that should lend weight to his words. I know that there is no authority but truth, and that not the word of an angel from heaven can make black white. That combination of prejudice and ignorance which has played such a part in human history prevented our opponents from listening even to facts: neither would they be persuaded though many rose, if not from the dead, at any rate from what promised to be their death-bed. But critics of that type are just the very persons who will blindly follow authority, and thus a new stage in this matter was reached when it was taken up by the great man of science whose contributions to it I am about to discuss. Prof. Ernst Von Leyden was, until a few months ago, the Professor of Clinical Medicine in the University of Berlin, and his name is familiar all the world over to students of the medical sciences. He is also the head of the Official Cancer Research of the German Empire, and as such is certainly the foremost official authority upon malignant disease in the whole world. Had I had the power, I

should naturally have chosen him, of all men, to lend the weight of his name and reputation and position to the unbiased and thorough study of Dr. Beard's pancreatic treatment of cancer. Prof. Von Leyden has at his disposal the unrivaled resources of the great Institute for the study of cancer which he controls—resources not only in money and apparatus, but in the form of a staff of highly-skilled experts. Various aspects of the question are now being worked at by him and his followers, and I have little doubt that, not long after these words appear in print, the practical application of Dr. Beard's discoveries in Germany will afford an object-lesson to the whole world. It is so now with the case of the English pioneer whom we name Jenner, the English pioneer whom we name Lister, and the French pioneer whom we name Pasteur.

More than two years ago, Prof. Blumenthal, Von Leyden's chief assistant, demonstrated that "all carcinomata (cancers) are always very easily digested by pancreatin (extract of pancreas), whilst on the contrary, all other tissues of the organism are fairly resistant to its action." This, of course, refers to test-tube experiments upon dead tissues. Pepsin, on the contrary, had a very slow and imperfect action upon carcinoma in the test-tube. Later, Prof. Bergell, another distinguished physiological chemist of the German Cancer Research, proved that the native and characteristic albumin of cancer is easily digested by trypsin, but with difficulty by pepsin.

It was not until January, 1907, however, that Prof. Von Leyden gave us an indication of what we were to expect from him in the clinical direction, by a report in the *Zentralblatt für die gesämte Therap.* for that month. There he reported the case of a patient suffering from

cancer of the stomach who was treated with trypsin as well as by other means. On the 11th of December the patient was discharged from the hospital, the case being regarded as one of either great improvement or recovery. This I record merely for its historical interest. No amylopsin was employed, the preparation of trypsin must have been extremely imperfect, and I very much question whether the patient was cured. But at any rate this paper informed us that German science had now taken up the matter in its clinical aspect also.

Of far greater significance was the paper by Profs. Von Leyden and Bergell, published in the *Zeitschrift für klinische Medizin*, vol. 61, pp. 360-365, 1907. Here I will attempt to epitomize that paper in my own words. I need hardly say that I earnestly recommend a study of the original to the seriously interested reader. Hitherto it has been totally ignored by the *British Medical Journal*, despite my discussion of it in the *Daily Mail*, my references to it in the *Pall Mall Gazette*, the *Morning Post*, and the *Contemporary Review*, and my public indictment of the *Journal* in the *Observer*. It has been carefully epitomized and discussed in the *Journal of the American Medical Association*, and in France.

The authors begin by observing that the origin and growth of cancer is always strictly local. Its unlimited power of growth has ever been its most striking symptom, and a most marked feature of it is that the tumor responds by increased growth to all forms of mechanical or chemical injury, or injury by heat, hitherto known. We, therefore, are compelled to suppose that the really important fact for us to ascertain about cancer is not, let us say, the shape of the cells, but their chemistry. What peculiar facts are there about the chemistry of cancer which con-

stitute the essential difference between it and normal tissues? Such facts there must be, and, accordingly, it must be possible, in theory, to exercise a special action on the chemistry of cancer, which will arrest its living processes but will not affect the chemistry of normal tissues. Prof. Von Leyden insists that we must abandon as of central importance the study of the appearance of cancer to the naked eye and under the microscope. For half a century this study has constituted practically the whole of cancer research. Medical chemistry, during all this period, was far too imperfect to be of any avail. The real question is, What sorts of substances are formed by malignant tumors, whose growth we are not able to stay? Now the authors point out that the only substances found in living matter which show a far-reaching specific nature—that is to say, a wide distinctness from each other—are the albumins, such as white of egg and the albumin of milk. Secondly, the various ferments which destroy these albumins are equally special in their properties; probably they differ from one another in precisely the same degree as do the albumins which it is their business to pull down. The question then arises whether there are unique albuminous substances in cancers—whether the albumins of malignant growths are substances which differ in build and composition from the molecules of the other albumins. This question has already been answered definitely by Bergell and Dörpinghaus, says Von Leyden, who have separated peculiar and characteristic albumins from mouse-cancer. Prof. Von Leyden insists that the existence of these special albumins is absolutely characteristic of malignant tumors, as distinguished from innocent tumors and normal tissues. The further question whether these special albumins can be specially destroyed has al-

ready been answered, as I have said; thus confirming what, on theoretical grounds, Dr. Beard declared must be so, on December 13, 1904, and what I myself have been asserting, on the grounds of Dr. Beard's theory and my own clinical observation, since March, 1906.

Prof. Von Leyden then goes on to point out the bearing that these observations of his have upon the theory of Dr. Beard and his experiments on cancerous mice. In the light of these experiments, and fortified by the observation of Blumenthal, he determined to go very closely into the clinical investigation of the new remedy. Large quantities of the ferments would have to be employed, Von Leyden thought, and he refers to the experiments of Billroth, who, some years ago, made hypodermic injections of iodine, quinine, and some other substances, in cases of cancer, without any result. Von Leyden set himself to prove that when trypsin was given by the mouth, a certain quantity of it actually passed into the blood. He found with certainty that trypsin, given by the mouth, could, to some extent, be recovered in the urine, and he came to the conclusion that by mouth administration it is possible to bring much larger amounts of trypsin into the circulation than by subcutaneous injection. But on this point Prof. Von Leyden has probably already found occasion to revise his opinion. We must remember that he was using injections made from dried trypsin, and I have no doubt that those which he employed were practically impotent, compared with the best injections now on the market. It has to be remembered, also, that in whatever dose trypsin be given by the mouth, its exposure to the normal acid of the stomach will destroy it, and only by very careful administration, **at** a time when it is probable that the stomach contains

no acid, can it be hoped to pass on undestroyed. It would be much to be regretted if the great name of Von Leyden were to encourage practitioners to place in the administration of trypsin by the mouth an amount of confidence which I am not certain that it will repay. In the patients whom Prof. Von Leyden treated there were reasons which would explain, I believe, why the trypsin administered could escape destruction in the stomach, because these were cases of cancer of the stomach, in which it is known that the organ no longer produces its normal acid. Therefore, I would strongly insist that this paper of Prof. Von Leyden's, as he doubtless would himself admit, by no means definitely proves that any very substantial value is, at present, to be attached to the administration of trypsin by the mouth. Would that one could say otherwise—as perhaps may yet be said—for if the mouth administration were really effective, nearly all the difficulties against which we are struggling would disappear at once with the disappearance of the need for making any injections at all.

Nevertheless we must not under-estimate the importance of the positive demonstration that trypsin given by the mouth can be absorbed into the blood. This fact affects us as regards both practice and theory. It shows that the oral administration of the ferments—for we may provisionally assume that what Von Leyden has proved for trypsin will be true of amylopsin also—is perhaps not to be relegated to a position quite so subsidiary as I have hitherto allotted to it. Whilst, on the other hand, I desire to avoid any statements which will lead the practitioner to regard the use of the hypodermic method as non-essential—for I doubt whether by any other means we can introduce so much trypsin into the blood—yet, on the

other hand, I am well aware of the vast advantages of oral administration, both as regards the difficulties of the manufacturing chemists, and as regards the convenience and ease and safety of the patient. By mouth administration it is possible to give practically unlimited quantities of the active ferments, without risk of abscesses caused by dirty methods, or of destroying the ferment by otherwise faulty technique. The first patient I saw, who, like many others, declined to continue with injections which at that time (February, 1906) were very painful, might conceivably have been saved if the mouth administration had been pushed. Let it be remembered in practice, therefore, that considerable quantities of the active ferments can be introduced into the blood, and therefore necessarily be brought to bear upon the growth, by mouth administration. In cases of, for instance, rapidly growing and highly malignant sarcoma, this possibility, superadded to the hypodermic method, may turn the scale in the patient's favor. We are dealing not with a poison—to the patient—but with a literally native inhabitant of the normal body; and if a desperate disease can be controlled by a remedy so far from desperate, we must use every channel in our power for its application. It is to be doubted whether the use of keratin or other capsules, which the gastric juice cannot digest, is advisable, since not infrequently the digestive processes of the bowel fail to digest the capsule, and the remedy is wasted. It is possible that this is especially liable to occur in cases of cancer, since the pancreatic secretion, upon which we rely to digest the keratin, may be defective. The method, then, as I have already stated, must be to give large—very large—doses of the ferments before meals, when it is practically certain that the gastric

contents are not acid, but neutral or faintly alkaline. The difficulty of passing the ferments undestroyed through the stomach is undoubtedly less in cancer than in other diseases or in health, since recent observations show that the secretion of hydrochloric acid by the stomach is diminished or abolished not only in cases of cancer of the stomach—as has long been known—but in cases of cancer generally. I submit, then, that what I have said formerly as to the mouth administration of the ferments must not be considered without reference to Von Leyden's recent demonstration that active trypsin can be recovered from the urine after administration by the mouth.

But this demonstration is also of very considerable theoretical importance; and though the primary object of this book is therapeutic and practical, we may briefly consider this point here. If trypsin reaching the bowel from the stomach can be absorbed—the physiology of the stomach making it almost certain that the remedy is not absorbed directly through the gastric wall into the blood—then we know, for certain, that the trypsin normally formed in the bowel by the fermentation of the pancreatic trypsinogen by the intestinal enterokinase, can also be absorbed: I do not say is absorbed, but can be absorbed. Are we to suppose, then, that this normally occurs to any appreciable extent?—or that it only so occurs when, as presumably in the observations of Von Leyden, the bowel contains an excess of trypsin? These questions are really momentous. They suggest the possibility that there may be some truth in the speculation of a former chapter regarding the greater absorption of trypsin from what I have called the "Fletcherite bowel"; and they also lead us to ask whether the age incidence of cancer has any

dependence upon a conceivable though quite unproved diminution in the activity of the pancreas. It may be that the jagged tooth of a young man arouses no cancer in his tongue, though there is present there the aberrant germ-cell which, similarly irritated thirty years later, would almost surely develop into a cancer—because the young man is protected by the trypsin absorbed in adequate quantity from a bowel supplied by a vigorous young pancreas.

At any rate, it is to be recognized that whatever factor—diet or youth or any other—facilitates or permits the absorption of trypsin from the bowel, is a factor directly tending, on Dr. Beard's theory of the specific toxic action of trypsin on cancer, now absolutely established, to prevent the occurrence of cancer. *Per contra*, any factor, such as overeating with intestinal decomposition, or senile debility of the pancreas, which interferes with such absorption, removes a condition which inhibits the growth of cancer, and thus predisposes to it.

Plainly there is a great field here for immediate physiological research. Is trypsin normally present as one of the ferments of the blood? The probable answer is affirmative. I am well aware that in previous writings I have advanced arguments which tend to the opposite conclusion. That matters nothing, for my opinion, like all opinions, settles nothing, alters no truth: I can merely state what I believe to be facts and arguments which I believe to be valid so far. If the reader is dissatisfied let him investigate the matter and instruct us all. My own opinion is now tending to the view that trypsin may—and perhaps *should*—normally be absorbed from the bowel, and should therefore be a normal inhabitant of the blood, rapidly excreted by the kidneys, no doubt, but

rapidly replaced, during the daytime at any rate. For if trypsin be normally present in the blood, perhaps only in minute quantities, its percentage must fall to zero after a longer or shorter period of fasting, when no more is being produced, while its excretion by the kidneys continues. Here is a further opportunity for the young physiologist.

The three considerations which support the case for the normal presence of trypsin in the blood are now, I think, as follows. First: it would have a value and function in the blood as a preventive of cancer, whilst formerly, of course, we knew it simply as a ferment produced in the bowel for the needs of the bowel alone. Second: when large doses of trypsin are given by the mouth, it enters the blood, as Von Leyden has shown. Third: the injection of normal pig's blood, freed from its cells and fibrin, under the skin of cancer-patients, has been proved to exercise a marked and unmistakable control over the disease. This is the recent work of Prof. Bier, which falls to be discussed later in this chapter.

Even if trypsin be normally present in the blood, it by no means follows that it usually there occurs to such an extent and so continuously as to protect us adequately against cancer—at any rate in man, whose digestive glands are doubtless less active than those of such an animal as the pig.

After this long digression, necessitated by the importance of Von Leyden's observation, we must return to the study of his admirable paper.

Though, as I believe, Prof. Von Leyden's method of applying the treatment was very far from satisfactory, he has convinced himself, and asserts in this paper as a proved fact, that without doubt circumscribed regions

of cancer can be successfully digested by trypsin injected directly into the tumor. The point is, of course, important, whether the action is one of true specific digestion, and Prof. Von Leyden promises us shortly a paper by one of his followers which proves that the influence of trypsin on the growths was true ferment action and not confused with bacterial disintegration. He goes on to say that his results are inferior to those which might have been expected from the work of Prof. Morton. That is undoubtedly so. But I believe inferior results will continue to be obtained until it is realized that hypodermic injection is the essential method—at present, at any rate. Prof. Von Leyden has given very large doses of trypsin by the mouth for months in various cases of internal cancer, and has nothing definite to report. I doubt whether in such cases any appreciable portion of active trypsin ever approached the site of the disease. No matter how large the dose and how active when given, the acid juices of the stomach—which is seldom entirely free from hydrochloric acid in such cases—would probably destroy it, unless the trypsin was given with such special precautions as wrapping it up in something which the gastric juices cannot dissolve. But Prof. Von Leyden goes on to say that, in almost every instance, suitable cases of gastric cancer reacted favorably to the treatment, and he is prepared to admit, despite the imperfection of his results, that there is here a curative influence which must be recognized. In the course of his investigations he has brought out, he tells us, an absolutely new fact. Perhaps it is new so far as demonstration is concerned, but Dr. Beard and I have been proclaiming it for a long time past. The author reminds us of what he began by saying—that malignant tumors sub-

sequently react by increased growth after the application of any injurious agent. But in trypsin he finds the single and all-important exception. Never has a tumor, after partial dissolution of its cells by trypsin, subsequently reacted by increased growth, either locally or generally. The point is that while scores of substances will injure a malignant tumor, such as the surgeon's knife, and pastes containing arsenic and other caustics, here in trypsin is an agent, injurious to cancer like them, but differing from all others in that, after its use, the tumor (assuming that it has not all been destroyed) does not respond with increased growth. Let me add for myself a second point which should be bracketed with this, and which Prof. Von Leyden himself suggests by his reference to the specific action of radio-active substances. It seems to be quite certain that the Röntgen rays, radium, and the allied substances have a specific relation to cancer in that they will affect it more rapidly than normal tissues; but in trypsin there has been found a substance which, whilst specifically digesting and destroying malignant tissues, whether living or dead, *has no action whatever, in any dose, on normal living tissues.*

I have already ventured to offer criticism upon the amount of stress which Prof. Von Leyden is inclined to lay upon the use of trypsin by the mouth, and I must also allude to the fact that, up to the publication of this paper, Prof. Von Leyden had taken no cognizance of amylopsin. Now, except possibly in the most superficial cases, I do not believe that trypsin alone will ever cure cancer. No one yet has recorded a case of the cure of cancer by trypsin alone. The actual cures already reported have been obtained, without exception, by the use of trypsin and amylopsin.

The very next paper in the journal to which I have already given the reference deals conclusively with a most important matter, and what appeared to be a most serious objection, cutting at the very root of Dr. Beard's theory. For more than a year past I have been much perturbed by the very definite statements made in the most recent text-books of physiology that when ferments, including trypsin, are injected into a living animal, there is promptly formed in its blood in each case an anti-ferment which protects the animal and prevents the substance injected from having any action whatever. I could not actually believe this of trypsin: in the first place, because of the results obtained by its use, and, in the second place, because it is a native inhabitant of the body of every one of us, and it seemed incredible that, even if it is not normally absorbed from the bowel, the blood should treat it as an enemy and a poison. Now this treatment during the past eighteen months has suffered greatly at the hands of critics, of whom I have already spoken in plain words. I will offer just one proof of the ignorance of these critics—ignorance not discreditable to any one who remained silent, but absolutely inexcusable in those who, knowing nothing, have dared to denounce this treatment. During all this time not a single opponent anywhere has offered what has hitherto been the one really substantiated argument against the treatment—namely, the statement of the physiologists that trypsin injected into the blood would be immediately neutralized. It was not my business to draw the attention of the critics to this argument, since I did not myself believe it, but I present them with it now with much pleasure, and with the answer to it.¹ Drs.

¹I drew attention to this point in the *Daily Mail* first of all. If

Schütze and Bergell have made experiments on rabbits extending for months, and have repeated those made in previous years by other observers. They find that all plant-ferments when injected into a rabbit produce anti-ferments. They find that pepsin injected into a rabbit produces an anti-pepsin, a fact which any one might have predicted from Dr. Beard's embryological work of twelve or fifteen years ago. But they find that trypsin injected into the rabbit never produces any anti-substances at all. The anti-trypsin, then, of which the books speak do not exist, though I do not say that an anti-substance might not be formed if trypsin were injected into a plant. Let the reader observe the contrast between pepsin and trypsin in this respect, and also the contrast already mentioned between pepsin and trypsin in respect of their action upon cancerous tissue in the test-tube. All these facts fit in absolutely with Dr. Beard's theory of the trophoblastic nature of cancer, and the fundamental antagonism between pepsin and trypsin in the history of the development of the body. That this research should have been undertaken clearly shows what progress we may expect now that the work of Dr. Beard has been taken up in the great city and by the great students who lead the medical science of the world. At the same time it will stand permanently on record that the first great results in human patients were obtained by American physicians.

The next contribution of Prof. Von Leyden—with Dr. Bergell—to this subject is to be found in the *Deutsche*

the reader is surprised that I thought this matter suitable for the popular press, let me remind him that I should have written in the *Hibbert Journal* or the *Police News* had I had the opportunity of doing so. Readers of both die of cancer.

Medizinische Wochenschrift, 1907, No. 23, p. 913. At the moment of writing it is of course impossible to say what the results of this new development will be. We may remind ourselves that Von Leyden had been using preparations made from dried trypsin, and had employed no amylopsin. The results he obtained were very far from being ideal, but there were definite results. It has proved that certain ferments were capable of specifically attacking the specific albumins of malignant growths, and this without any subsequent reaction on the part of the growth. In the absence, however, of ideal results, Prof. Von Leyden set himself to ascertain whether any other organ of the body would yield a ferment still more effective than trypsin—or, rather, still more effective than the preparations of trypsin which he employed. We may take it that at this point the feasibility and the scientific reasonableness of treating cancer by ferments, as originally suggested by Dr. Beard, was definitely established in his mind; and it was the liver in which he thought it possible to find a ferment more potent or of wider applicability than trypsin. He obtained, then, from the livers of animals a ferment (prepared as a semi-solid substance and incapable of being injected) which, according to him, possesses the power of dissolving certain peptones which are not attacked by trypsin. (In point of fact, an intra-cellular proteolytic ferment had already been found in the liver by Jacoby.) This substance was introduced by means of a spatula into the substance of three highly malignant tumors. In each case the malignant mass was dissolved with such rapidity and energy that the reporters compared the action to that of nitro-glycerine—reminding us of a former comparison between trypsin and dynamite. So powerful,

according to them, was the action, accompanied as it was by the formation of poisonous substances, that at the time of publication of this paper the authors were concerning themselves with the discovery of means by which it could be regulated for practical use in the treatment of cancer.

The authors declare that the liver-ferment in question has an action even more powerful than that of trypsin upon the cancerous cell and its albumins. Further, they declare that this ferment acts with far more power upon living cancer than upon cancerous tissue in the test-tube—upon cancer *in vivo* than upon cancer *in vitro*: a statement all but incredible. The authors further suggest that the power of growth of cancer depends upon the absence of this ferment from the body of the cancerous patient.

The summary of the paper in question is as follows, as accurately as possible: The proteids of cancer—or “proteins,” to use the modern phraseology—are specific albuminous substances of which the destruction by dissolution demands the intervention of agents possessing a specific action upon them. Secondly, of these agents, which belong to the group of ferments, one which is particularly active can be obtained from the liver. Its disappearance from the body of the cancerous patient permits a new growth to multiply and increase without obstruction. The employment of this ferment in the treatment of cancer seems to be possible.

Now what is to be said at the present stage regarding these latest recorded results obtained by Prof. Von Leyden? Assuming that no trypsin in any form is used in the cases in question, we may take it that there can be obtained from the liver a ferment which has a specific

action upon cancer. It seems to me not inconceivable that this ferment may actually be trypsin or a form of it, possibly absorbed from the bowel after its formation there, and reaching the liver in the ordinary way. It will require to be demonstrated that this substance is not trypsin. A weakly acting tryptic ferment was found some time ago in bile by Bruno and by Tschermak. The next question that arises is as to its superiority—assuming it to be different—to trypsin for the purpose in question. There is, of course, no *a priori* impossibility that it should be superior, still less that there should be more ferments than one which can act upon a given albumin or group of albumins, just as both pepsin and trypsin will digest certain albumins, or just as both the ptyalin of the saliva and amylopsin will digest certain carbohydrates. If, then, a ferment more powerful than trypsin has been discovered, and if it can be employed in such a fashion as to avoid the formation of an excessive amount of poisonous products, so much the better.

But at the present time I am inclined to question these conclusions. In the first place, Prof. Von Leyden has been comparing this liver-ferment—which, for the moment, we may assume to be distinct from trypsin—with injections made from dried trypsin, the potency of which was not estimated in digestive units; but, if we may judge from what we know of dried trypsin as a basis for injections, was probably very low. Secondly, Prof. Von Leyden employed no amylopsin. This ferment has been declared by all who have reported on it—the Middlesex Hospital observers excepted—to control the toxic symptoms which may be induced by the use of active trypsin in cases of cancer. Quite possibly it would have controlled the toxic symptoms induced by the use of this

liver-ferment, the toxic substances being in all probability identical, or nearly so, since in both cases they are the results of the action of a proteolytic ferment upon the characteristic proteids of cancer.

There remains the theory formulated by Prof. Von Leyden and Dr. Bergell, that it is the absence of this ferment from the liver that permits the growth of cancer in any given case. This question of the causation of the cell-multiplication we call cancer is a most difficult one, to which Dr. Beard has declined to offer any answer, and Prof. Von Leyden's answer to it evidently does not affect either in one direction or the other the validity of Dr. Beard's theory as to the trophoblastic nature of malignant tissue, and its origin in an aberrant germ-cell. This theory involves no statement as to the conditions which induce the germ-cell to multiply in the first place, nor as to the conditions which permit its multiplication to proceed unchecked when it has for some cause or other been induced. Each of these is a question still awaiting an answer. If it be that Prof. Von Leyden has found the answer to the second of them, so much the better. The validity of his answer is evidently capable of rapid proof or disproof, since it would appear to involve nothing more than the chemical examination of the liver in cases of persons who have died from cancer. If it be found impossible in such cases to extract this ferment from the liver, then a fact of the greatest importance will apparently have been discovered in the elucidation of the conditions which permit the growth of cancer. I confess at the moment to much doubt that this result will be obtained. I also confess to much doubt whether the use of this liver-ferment—though it seems at present impossible, in the face of Prof. Von Leyden's authority, to ques-

tion its specific action upon cancer—will be found as safe as or efficient as the use of really active preparations of trypsin and amylopsin.

Such, at any rate, at the time of writing, is Prof. Von Leyden's contribution to this subject. Its value as confirmation of the results already obtained elsewhere is incontestable, and it remains to be seen how much there is in it which constitutes a positive advance upon the work previously done. But though his was the most important of the earlier German papers on this subject, and though I have naturally used his name and authority since last June, both in England and America, in the effort to gain a fair hearing for the new treatment, there can be little doubt that certain other workers in Berlin have made contributions to it of equal or greater weight, and these must now be discussed.

It is worthy of note, in passing from the work of Von Leyden, that he has hitherto been the chief living exponent of the parasitic theory of cancer—the theory that the disease is due to the invasion of the body by minute parasites, as are so many other diseases. Prof. Von Leyden, who is now seventy-five years of age and has retired from his Chair since his work with ferments was published, has set younger men a fine example in abandoning his long-held views and accepting a totally new series of conceptions in regard to the nature, and therefore the treatment, of cancer.

Prof. Bier, who holds the Chair of Surgery in the University of Berlin, the foremost surgical Chair in the world, is noteworthy as by far the most distinguished surgeon—indeed the only distinguished surgeon—who has yet addressed himself to the treatment of malignant tumors by ferments. His method of treating various

forms of local tuberculosis, especially of the joints, by stemming the return of the blood from the diseased part through the veins, is known and practiced all over the civilized world. He attributes the utility of this method to the increase in the number of white blood-cells which are thus brought to bear upon the invading bacilli. It is possible that the British surgeons who have so consistently declined to attend to Dr. Beard, a British embryologist, or even to Prof. Von Leyden, a foreign physician, may listen to one of the most famous and highly placed members of their own craft.

In the *Deutsche Medizinische Wochenschrift*, July 18, 1907, there appeared a paper by Prof. Bier, the publication of which was hastened by the previous appearance of Von Leyden's contributions to this subject. Some years ago Prof. Bier obtained very remarkable results from the treatment of a case of multiple sarcoma by the injection of blood, and this was the method employed in his recent experiments. He mainly employed the blood of the pig—a fact which especially interests us, as will be seen—and the injections consisted of from ten to twenty cubic centimeters of blood, previously freed from its white cells, and from the constituent called "fibrinogen," which clots into "fibrin" when blood is drawn, under the action of the fibrin-ferment formed by the white blood-cells. This very large and inconvenient dose of "defibrinated" blood was injected subcutaneously—of course with minute precautions, especially necessary with this method, to prevent abscess-formation or other infection by microbes. Marked local and general symptoms of inflammation follow this procedure, lasting for some days; and such blood-cells as remain in the injected blood are destroyed, together with many of the blood-cells of

the patient. This result of the injection into one animal of blood from another species of animal has, of course, long been known. No actual disasters occurred, though the process must have been extremely painful and unpleasant, besides destroying part of the patients' blood. Nevertheless the normal tissues of the patients were not injured in any way, any more than they are by the injection of even strong solutions of trypsin or amylopsin.

Highly remarkable and characteristic changes were observed, however, in the malignant tumors from which the various patients were suffering. As with the ordinary pancreatic treatment, pain was relieved, discharge was checked, and the process of local death and necrosis of the surface of the exposed tumors was arrested. But in several instances much more was observed: the tumors appeared to die and degenerate as a whole, and gradually diminished instead of increasing in bulk. In more than one instance something not far short of an actual cure was obtained. Sometimes the growth dried up and died, even in advanced cases, and the cancerous cells disappeared—neither ulceration nor the sloughing of merely dead cancer-tissue occurring. In other cases, there was not so much an exodus of the growth as its replacement by innocent fibrous tissue. In a word, the results were apparently similar in detail and variety to those observed by the earlier experimenters with trypsin and amylopsin, and especially in those early cases in which amylopsin was scarcely employed at all. The specific or selective action of the remedy, killing the malignant tissues and not affecting the normal tissues, is specially to be noted as familiar to the experience of Dr. Beard's followers.

Prof. Bier fully recognizes that these results, which, had they been obtained and published two years ago,

would have been unparalleled, were obtained by the action upon the living cells of the tumors, of a ferment or ferments contained in the blood. Obviously no other interpretation of the facts would be possible, even if these results were unprecedented. At the very least, then, they furnish yet one more independent piece of evidence, contributed by one of the very first of living surgeons, of the fact that it is possible to control the growth and even the life of malignant tumors by a ferment or ferments which exercise a strictly selective and, in this respect at least, ideal action, injuring only the tissues which are injuring the patient. A year ago such results as these would have been invaluable to me as an argument for Dr. Beard's cases; and even to-day they may be commended to all concerned as positive evidence contributed by a great surgeon, and obtained in a quite novel fashion, of the main thesis of this book—that ferments exist which can control the growth and life of cancer without injury to normal tissues.

Before we consider the more theoretical significance of these experiments, it is necessary to look at them from the practical standpoint. We must note, then, that Bier's method of employing ferments has not hitherto obtained results in any way superior to those obtained by the previous method. Further, the injections cause much local and general disturbance and destruction of certain elements of the patient's blood; and the bulk of fluid injected is very large. I have little doubt that the ten or twenty cubic centimeters of pig's blood used by Prof. Bier, if estimated in digestive units, would be found far less potent than is, for instance, one cubic centimeter—the usual dose—of the medium strength injection of Messrs. Squire & Sons, this containing five hundred units

(Roberts) of proteolytic and two hundred of amylolytic activity. We may well believe that Prof. Bier is doubtful of obtaining cures by this method, though, on grounds about to be discussed, I dare say that if the pigs be fed for weeks on proteid food, and the blood be drawn about three hours after a large proteid meal, a higher concentration of ferments will be obtained. But even so, neither the general features nor the results of this method make it likely, perhaps, that it will prove more effective than the pancreatic treatment as hitherto practiced in the best hands.

Turning now to the theoretical questions involved in these valuable experiments, we must inquire into the origin and, if possible, the nature, of these ferments to which Prof. Bier attributes his results. We may agree with him that the blood is both a carrier and a producer of ferments. It is known that the white cells, aided by the presence of lime-salts, are able, when stimulated, to clot the blood by the formation of the "fibrin-ferment." Prof. Metchnikoff's great researches into the function of the white cells also suggest that they are capable of producing other substances, many or all of them ferments, which can destroy the microbes of disease. But we are without evidence of the *external* production of any proteolytic ferment by the white cells, though they must contain, *within themselves*, such a ferment in order to digest their own food. The only other living elements of the blood, the red cells, are purely respiratory in function, acting as oxygen-carriers, and though they conceivably produce a respiratory ferment, no one will credit them with further powers in this direction. The white cells were removed from the blood injected by Prof. Bier, and the red cells were speedily destroyed, as are alien

cells in general when they enter the blood. We may, therefore, with practical certainty exclude the blood itself as the source of the ferment or ferments which destroyed the cancer-cells of Prof. Bier's patients.

It is well to remember that, though pathologists and clinicians most misleadingly speak of "diseases of the blood," and though this fluid is too commonly regarded by many as if it were an immediate product of the universal ether, in reality all the living cells of the blood are made elsewhere, in various glands and in the red bone-marrow, whilst its fluid part, like all the fluids of the body, is a cell-product, except in so far as it is directly derived from the food. Now, the blood being a ferment-carrier, as Prof. Bier says, and the origin in itself of its cancer-destroying ferment or ferments being, perhaps, excluded, we must look elsewhere for their source.

Von Leyden, Schütze and Bergell have lately taught us that trypsin is capable of absorption from the bowel, and that when it is injected into the blood it is treated not as a stranger but as a native. The blood reacts to all foreign substances without exception, but it does not react to trypsin. Thus the probability is extremely high that trypsin, formed in the bowel of the pig from the trypsinogen of its pancreas, is, in part, at any rate, absorbed into the blood. The pig must not be credited with the unwise dietary habits of civilized man, which provide him with a rich "intestinal flora" that may well prevent the absorption of much trypsin, if any, from his bowel. Further, the pig, with whose blood most of Prof. Bier's results were obtained, has a very highly active pancreas; and whilst he was relieving cancer-patients by means of the ferments contained in the blood of the pig, Drs. Pinkuss and Pinkus, and many others, were obtaining

similar or better results by the use of injections made from the pancreas of the pig, which is the animal chiefly employed, on account of the activity of its pancreas, as a source of the pancreatic ferments.

Lastly, we have to remember the highly specific character of ferment action, and the fact that trypsin, at any rate, is one specific ferment for the peculiar albumins of cancer. Elsewhere I have noted Dr. Beard's argument from the vast antiquity of trypsin in the evolution of the animal kingdom.

When all these considerations are appraised, it seems highly probable that the active ferment of the pigs' blood used by Prof. Bier was none other than the trypsin formed from the pancreatic trypsinogen in its bowel and thence absorbed into its blood. This is why we may surmise that the blood will be found more actively cancrotoxic should Prof. Bier take steps to heighten the activity of the pig's pancreas by modifying its diet, and to obtain the blood when it is most likely to contain its maximum amount of trypsin.

The same argument applies to the other animals with whose less effective blood Prof. Bier experimented; but the special fitness of the pig for his purposes offers a suggestive coincidence with the similar fitness of which the chemists avail themselves in the preparation of trypsin.

We know that cancer does occur, though with relative rarity, among vertebrates generally, but in view of the known activity of the pig's pancreas, and of Prof. Bier's results, it would be interesting to know to what extent cancer has been observed in the pig, while the pancreas should be examined *post mortem* in any cases that may hereafter be observed. Dr. Beard informs me that,

so far as he knows, no case of cancer, or of identical twins, has been recorded in the pig.

The possibility, then, is that Prof. Bier's methods simply constitute a variety of the pancreatic treatment, and one characterized, so far, by no specially favorable results to compensate for its very numerous and serious disadvantages for all concerned—the practitioner, the patient, and the pig.

It is conceivable, of course, that the cancrotoxic ferment of pigs' blood may not be trypsin, but may be a closely allied ferment produced in some other organ than the pancreas. This possibility is perhaps the less improbable since Von Leyden and Bergell have apparently isolated a cancrotoxic ferment from the liver. Possibly the blood-ferment is one and the same as the liver-ferment, and possibly trypsin is the real name of both; possibly all three are distinct.

Here I may note that, though Dr. Beard was led to indicate the use of ferments in cancer, and to indicate trypsin in the first place, because he observed the coincidence in time between the degeneration of trophoblast and the commencing activity of the pancreatic cells in normal development, there is no *a priori* reason why the liver or the thymus,² or, indeed, any other gland, should not also produce a similar ferment. It will remain for a more advanced chemistry to inform us as to the composition and structure and relations—or possible identity—of such cancrotoxic ferments as have hitherto been, or in the future may be, discovered. If such ferments, other than trypsin, are discovered, and made capable of therapeutic

²In the *Annals of Surgery* (Philadelphia, July, 1907) Dr. Gwyer reported favorable results from the use of the thymus-gland in cancer.

employment, and if they prove more potent than trypsin, and not less safe, then so much the better. I hope that neither of Dr. Beard nor myself may it be said that we "mistake the horizon for the end of the world"; the close of the first or pre-scientific epoch in the history of the treatment of cancer is doubtless only the opening of another, controlled by the rational pathology and biological chemistry of Dr. Beard's conception.

Before leaving Prof. Bier's work, I must briefly discuss a further consideration to which it gives rise. If pig's blood and lamb's blood, for instance, are cancrotoxic, why should not human blood be cancrotoxic also? The affirmative answer does not necessarily follow by any means, since it is conceivable that the crucial factor in Dr. Bier's experiments was the employment of alien or "heterologous" blood. This, however, is, I think, extremely improbable. On the contrary, it may be expected, in my judgment, that the employment of, say, human blood derived from a *young* person accustomed to abundant and coarse proteid food, and possessed of excellent digestive powers, would prove as effective as the blood of the pig. Plainly this experiment will have to be made; unless, indeed, it should become evident that, with our present knowledge, this method of employing the ferment treatment in human patients is no longer legitimate.

The recent German work includes a great deal of research upon the chemistry of cancer and the nature of the cancerous cell. This work affords the most striking confirmation of Dr. Beard's contentions, and it must be discussed here, however briefly. But meanwhile it is my object to present to the reader, in order of publication, the *clinical* work which has been accomplished in

the treatment of cancer by specific ferments, whatever their real or apparent source; and in following this plan we now have to consider what, in my opinion, is certainly the most exhaustive and valuable, as well as the most recent, of the German contributions to the clinical aspect of this subject. In this case there is no doubt as to the nature of the ferments employed.

The paper in question appeared in the *Medizinische Klinik*, Nos. 28 and 29, 1907. This weekly journal can boast the most illustrious direction of any now extant, the names including Profs. Brandenburg, Bier, Von Leyden, Ehrlich, Fraenkel, Gaffky, Von Mering, Neisser and Verworn, whose names are all permanently recorded in the history of medical science; and the allotment of so much space to this paper is a sufficient index of the importance which is attached to it.³ The paper is entitled, "Die Krebskrankheit und ihre therapeutische Beeinflussung durch Fermente" (Cancer and its Therapeutic Control by Ferments), and the authors are Dr. A. Pinkuss, who is reporting secretary to the International Cancer Committee, as well as a distinguished clinician; and Dr. S. N. Pinkus, whose former experiments on the hypodermic administration of trypsin to dogs have already been mentioned. I will attempt to summarize the most important contents of this paper.

The authors begin by showing how Dr. Beard's embryological doctrines lead to the advocacy of trypsin and amylopsin for cancer, and they quote Von Leyden, Blumenthal and Bergell as holding that the chemical question is more important than the morphological one—*i.e.* the

³I note this point, since it bears upon the fact that it was left for me, "in the lay press" (*Contemporary Review*, September, 1907), to draw attention to this article in Great Britain.

question of microscopic appearances. They refer to Von Leyden's work, pointing out that, though locally effective, his procedure of making local injections *into* the tumors could not lead to really favorable results, because of its irrelevance to secondary growths. After communicating with Dr. Beard they determined to take up the use of the Fairchild preparations as suitable. Here I may note that their results were thus obtained with preparations necessarily deteriorated in some degree by the time occupied between their manufacture in New York and their employment in Berlin. The contrast between these results and those obtained by Von Leyden from preparations made from dried trypsin in Germany is all the more significant, as is the fact that any results were obtained at all.

Proceeding with the most admirable and scientific method, the authors first set themselves to prove the harmless character of the preparations, and for this purpose they made injections into many animals and into one of themselves. Five dogs, two guinea-pigs, one cat, and one rabbit were used. The following table gives the results:

Dog (4.6 kg.).....	5 c.c. inject. trypsin.
Guinea-pigs (220 and 280 grm.).....	1 c.c. " "
Cat (3.4 kg.).....	3 c.c. " "
Rabbit (1.3 kg.).....	3 c.c. " "

There were no abnormal appearances and no rise of temperature. Longer experiments were then made on several dogs and guinea-pigs.

Dog 2 (11 kg.)	recd. on 38 days 16 injections of 1 c.c.
" 3 (6.5 kg.)	recd. at irregular intervals 20 injections of 1 c.c.
" 4 (8.5 kg.)	} recd. for 4 weeks 1 grm. "holadin" ⁴ daily, and each 6 trypsin injections of 3 to 6 c.c.
" 5 (7.5 kg.)	

⁴This is a pancreatic preparation for oral use.

Two guinea-pigs (640 and 580 grm.) received in 24 days 16 injections of $\frac{1}{2}$ to 1 c.c. There was no fever nor local reaction noticeable. Dogs 3 and 5 were found to have all their organs normal, the pancreas and the bowel being microscopically examined.

Dogs 1, 2 and 4 were injected with sterile solutions of other ferment preparations, and with two *sterile* solutions prepared by the authors from somewhat decomposed pancreas-glands. Seven guinea-pigs also received these injections. In these cases one or two injections sufficed to raise the temperature markedly for long periods; there was marked local reaction, far-reaching necrosis, and five of the guinea-pigs and dog 4 died within ten days with all the symptoms of blood-poisoning. (*It is particularly to be noted that the solutions were sterile.*) In the other two dogs and two guinea-pigs, five injections of 1 cc. of "injectio amylopsini" (Fairchild) were followed by a lowering of the temperature and marked relief of the local symptoms, "whether *post hoc* or *propter hoc*."

The animals which received the Fairchild trypsin showed no anti-trypsin formation (cf. Schütze and Bergell), but those of the second series showed in their blood-serum more or less strong anti-tryptic properties.

In many of the above cases a tryptic ferment could be detected in the urine.

These experiments satisfied the authors that the Fairchild preparations were not poisonous, and this was confirmed by one of them, who made three injections into himself.

Now, say the authors, we could begin our experiments on cancerous human patients. Of course they confined themselves to cases where further operation was out of

the question. They began with some of their own cases, and two others handed over to them for treatment by Prof. Rinne in the Elizabeth Hospital, Berlin. This was three months before writing their present preliminary report. They got no abscesses⁵ and no necroses: the general condition of the patients did not suffer; on the contrary, usually their appetite and spirits were improved. Various reactions, such as fever, rigors and changes in the pulse occurred, but these were always found to disappear after some days' use of amylopsin. After various periods trypsin was found in the urine. The authors also studied the red matter and the white cells of the blood in these cases.

The following four cases are detailed by the authors:

Case 1.—Mrs. F. Inoperable “portio” cancer. September, 1906, curetted and treated with caustics. The patient had hæmorrhage and pain and foul-smelling discharge. Under the treatment the bleeding ceased, and the fœtor disappeared with remarkable rapidity; a healing process set in, and, at time of report, had been going on for nearly three months. The treatment was being continued. Trypsin was first found in the urine after 48 injections. (This is a remarkable and much to be considered observation, in my opinion.) The patient had her first rigor and fever after 42 days, and this was relieved after the use of amylopsin.

Case 2.—Mrs. W. Patient had worn a pessary for eight years, and had developed a “portio” (uterine) cancer. The womb had been extirpated, but the disease extended into the vagina. As a palliative measure, an injection of trypsin was made every third day. After the fourteenth injection rigor and fever appeared. The authors merely note this case as showing that the treatment is not harmful.

Case 3.—Male patient, age 58, having inoperable cancer of the left half of the face and the lower jaw, with secondary growths. The “X” rays had failed. The authors say: “In the last few days remarkably favorable changes, obvious to all observers, have taken place—softening of a nodule as

⁵Cf. the Middlesex Hospital results on this point and all others.

large as a cherry, disappearance of the swelling, decrease in the infiltration—that to-day we would reserve any critical judgment.”

Case 4.—Mrs. D., age 38. Cancer of breast of three years' duration. In January, 1907, operated upon, and for recurrence in April. Patient cachectic, suffering pain all over the body, and under morphine. Probably suffering from secondary growths in the abdomen and within the spinal column. This patient received daily injections, and after sixteen she has not yet shown any general reaction. The pains have ceased, the appetite is improved, less morphine is given.

The authors consider the preparations used by them much superior to those used by Von Leyden and Bergell. They are resolved not to be deterred, even if they experience some failures, and they say that they have taken up the treatment of further cases in the Elizabeth Hospital, Berlin. They recommend other physicians to take up the matter.⁶

The evidence almost daily accumulates to such an extent that this book is already twice as long as was planned when I began it a year ago; and I cannot afford further space to the consideration of this invaluable paper, which contains much more of importance than I have referred to. I pass now from the more especially clinical aspect of the German work to another which is less arresting, perhaps, but of the first importance nevertheless.

The most noteworthy of the recent German contributors to the more purely chemical aspect of the question, which must now claim us, is Prof. Ferdinand Blumenthal. At the end of the chapter will be found the references to his papers, the substance of which must now be stated.

He points out that until a few years ago—a very few in Great Britain—the pathologists regarded cancer in-

⁶If the student will read and compare this report with that of the Middlesex Hospital, he will wonder, I think, whether they really belong to the same age and the same planet.

vestigation as their exclusive domain. The minute structure of malignant tissue—*i.e.* the question of cell-shape, as I observe elsewhere—and the mode of formation of secondary growths were the chief things studied by them.

The cancer-cell is fundamentally different from a tissue-cell, Blumenthal asserts, on many grounds. He totally rejects the notion of Thiersch and so many after him that the cancer-cell has something degenerative about it. This is not so; and it is certainly not a degenerate form of tissue-cell. Prof. Blumenthal rejects the "embryonal" theory of Cohnheim, and mentions the parasitic theory, with which Prof. Von Leyden was so prominently associated until the work of Dr. Beard, followed by his own and that of his own assistants, led him to his present views.

Blumenthal finds no evidence of a "cancer-toxin" in the pressed juices of a cancer; but he refers to the "cancer-ferment" found by Petry, and observes that this ferment can be destroyed by the normal ferment found in the liver. This is to be noted in relation to Von Leyden's later work. But Blumenthal finds that the self-digestion of the liver (by its own ferment) is much aided by the addition of chopped-up cancer. Neuberg has also shown that the albumin of the lung is digested by the ferments of liver and cancer together. These results seem inconclusive, if not contradictory, and we may remind ourselves that cancer spreads frequently and grows very easily in the liver. Blumenthal attributes the cachexia, or general poisoning in cancer, to the entry of the cancer-ferment into the blood. But it has to be asked how far this cachexia occurs at all apart from bacterial infection and loss of blood.

Blumenthal goes on to show that in the albuminous

matter of cancer are found such substances as alanin, phenylalanin, aspartic acid and di-amino-acids, but very little leucin. We may note this in reference to the possible function of amylopsin as a destroyer of some of these compounds.

Blumenthal shows that pepsin digests dead cancer in the test-tube scarcely at all, while trypsin does so readily; and these results have been confirmed by Bergell and Dörpinghaus, and by Neuberg and Ascher. In his judgment this furnishes a chemical indication for the therapeutic use of trypsin in this disease. That further experience confirms this chemical verdict will be seen when we find Prof. Blumenthal saying later, at the Heidelberg Cancer Congress, September, 1906, that "the tryptic ferment extremely easily dissolves the cancer-cells, while the very opposite property is the case towards the other tissues"—*i.e.* the normal body tissues.

Blumenthal has also shown that the black pigment found in the tumors known as melano-sarcoma is not, as was assumed, the same as the melanin found in the normal body. In short, all Blumenthal's work goes to demonstrate a radical chemical difference between the cancer-cell and the normal epithelial cell.

In comment upon the foregoing, which constitutes the general results of Blumenthal's work, and the importance of which is none the less (though quite ignored) in Great Britain, shall we say, because the worker happens to live in Berlin rather than London, I must fix upon its most important statement, that of the specific digestive action of trypsin upon cancerous albumin in the test-tube. This, as such, furnishes warrant for a trypsin-therapeutics, according to Blumenthal; and it was this fact which determined Von Leyden to undertake his clinical inquiry. It

alone suffices not merely to recommend, but to *establish* the use of trypsin locally in the treatment of the dead cancerous tissue which is so lamentably familiar; whereof the admirable and rapid results may be observed by the least skilful and the most skeptical. I am absolutely certain that trypsin will be used for this purpose as long as cancer exists; its value, therefore, must be seen to be appreciated. But the vital question is as to the relevance of this exhaustively proved fact to the control of living cancer-cells. These indubitably contain the albumins which, when they are dead, trypsin so readily digests and destroys; and no one will question that their destruction in the living cell would entail its death. But the reader, whether biologist or layman, will recognize that, though the fact first noted by Blumenthal is conclusive as regards the palliative treatment of cancer, it is not conclusive as regards its curative treatment, even theoretically: the point involved being none other, indeed, than the difference, chemical, physical, electrical, or whatever it be, between life and death. For instance, the living cell, in virtue of its chemical activities, might have the power of digesting trypsin itself; and this might conceivably be effected by the cancer-ferment, if indeed it is not for some such "purpose" that this cancer-ferment exists. Now the "malignin" is present in the dead cell—it was originally found in the dead cell, and necessarily so; it does not there avert the action of trypsin; and on these grounds I would argue the probability, though *on these grounds* no more, that trypsin may pull down the albumins even of the living cell. The question as to the possibility of its reaching them therapeutically is answered by Von Leyden's demonstration of the passage of trypsin into the blood and its carriage there in an active state.

There can be little doubt that it can pass through the walls of the blood-vessels from within outwards—*i.e.* so as to reach the cancer-cells themselves, since we have proved that it can pass through them from without inwards—*i.e.* when it is absorbed. Here, however, the chemical work leaves us, having established one fact of very high importance, which just falls short of being the *capital* fact—*i.e.* the digestion of the living cell by trypsin.

I believe it should be quite possible, however, to determine even this, apart from clinical inquiry. Cancerous tissue can be removed and inoculated, as we know; in other words, it can live for a time apart from its host, of which it is no organic part, being indeed an independent organism of independent origin. It must be possible to experiment upon this living, though separated tissue, with fluids containing trypsin. Physiologists can keep separated organs alive for hours or days by means of an artificial circulation. Why should they not do the same with organs such as the uterus excised by the surgeon for cancer, and why should not the action of trypsin, added to the nutritive fluid circulated through such organs, be observed? There is room here for good and noteworthy work. Meanwhile, however, we have abundance of clinical evidence which shows more than such experiments at the most could show—namely, that cancer-cells in the living patient can have their specific albumin digested, and their death therefore effected, by the hypodermic administration of trypsin at a distance, if not, indeed, by its administration by the mouth, neither injection into the tumor nor injection directly into a vein being necessary for this result.⁷

⁷That is, as a rule. These methods may have their place in some cases. The latter has never been employed.

I would recommend further experimentation, which can involve little difficulty, with the cancer-ferment, and with the ferments of various cancers and sarcomas, if these differ, as I suspect they do. When these ferments are obtained in the test-tube, let us expose them to trypsin and observe the results. It may be predicted that, as a rule, if not invariably, the trypsin will be found to destroy the malignant ferments; but the reaction of the solution, whether alkaline—favoring trypsin—or neutral, or acid, will doubtless be found to be a factor of the greatest importance, probably greater than the question of concentration. It may be found that the results vary with the type of tumor from which the ferment is obtained, and with its history as regards stimulation by the surgeon's knife or other means. I believe that such experiments may lead, among other results, to valuable knowledge regarding the desirability of what seems to me possibly indicated, viz. the use of alkalies by the mouth in order, even if transiently, to increase the alkalinity of the body fluids, and reduce the acidity of the tumor fluids, thus aiding the curative and hindering the destructive ferment.

Such experiments may also explain—on the assumption of Blumenthal regarding the causation of cancer-cachexia—the consistently amazing influence of the pancreatic treatment upon the general state of cancer-patients, transforming their appearance and the value of their lives to themselves, abolishing the characteristic tint of the skin, creating appetite and increasing the body-weight. Hitherto I have inclined to attribute these results, which would alone suffice to make this the greatest step hitherto taken in the treatment of cancer, to the control of septic processes by the treatment; but it may

be that the cachexia of cancer is really a specific thing, and, if so, it is very likely due, as Blumenthal suggests, to the action of the cancer-ferment upon the blood and the tissues to which the blood carries it. On such a supposition the most likely explanation of the wholly unprecedented and unique action of trypsin in these cases is that it destroys by fermentation the cancer-ferment. This surmise should be capable of verification or refutation in the test-tube. With these considerations we may pass from the German work on this subject.⁸ It is highly characteristic of German science, it is by far the most important that has yet been done in the investigation of Dr. Beard's conceptions, and it is in striking and significant contrast to the scanty and purely clinical work which, except for the undescribed and unpublished and therefore scientifically negligible efforts of the Imperial Cancer Research Fund, is all that can be recorded in the "prophet's own country."

REFERENCES

- E. VON LEYDEN. Ueber die Probleme der Kurativen Behandlung der Karzinome (*Zeitschr. f. Krebsf.*, 1907, p. 161).
- E. VON LEYDEN and P. BERGELL. Verwendung des Trypsin (Pancreatin) bei Karzinom (*Zeitschr. f. klin. Med.*, 1907, vol. 61, p. 361).
- Ueber Pathogenese und ueber den spezifischen Abbau der Krebsgeschwülste (*Deutsche Med. Wochenschrift*, 1907, No. 23).
- A. BIER. *Deutsche Med. Wochenschrift*, July 18, 1907.

⁸At the time of writing (September, 1907), Drs. Pinkuss and Pinkus are making trial of the pancreatic treatment on a large scale in the Elizabeth Hospital, Berlin; prudence—or cowardice—would suggest waiting for their report, and doubtless it will be of great value, but as cancer will not hold its hand, I may not.

- A. PINKUSS and S. N. PINKUS. Die Krebskrankheit und ihre therapeutische Beeinflussung durch Fermente (*Medizinische Klinik*, Nos. 28-29, 1907).

PAPERS MORE ESPECIALLY CHEMICAL

- P. BERGELL. Zur Chemie der Krebsgeschwülste, in *Zeitschr. für Krebsforschung*, vol. 5, pp. 204-208. (Paper read before International Congress on Cancer, Heidelberg, Sept., 1906.)
- F. BLUMENTHAL. Die chemische Abartung der Zellen beim Krebs, in *Zeitschr. für Krebsforschung*, vol. 5, p. 183, 1907. (Also read before Inter. Cong. on Cancer, Sept., 1906.)

The above is a summary of—

Die chemische Vorgänge bei der Krebskrankheit, in *Ergebnisse der experimentellen Pathologie und Therapie*, vol. 1, pt. 1, 1907, pp. 65-104.

- NEUBERG and ASCHER, in *Arbeiten a.d. Pathologischen Institut zu Berlin*, 1906.

[All the above, except Prof. Bier, who has not used trypsin (as such), confirm the observation that trypsin has a specific toxic action upon cancer.]

For further recent references see the papers of Pinkuss and Pinkus, and of Blumenthal: also

- E. PETRY. Ein Beitrag zur Chemie maligner Geschwülste, in *Zeitschr. f. Physiol. Chem.*, 1899, p. 393.
- J. BEARD. Die Embryologie der Geschwülste, in *Deutsches Zentralblatt f. allg. Pathologie*, 1903, vol. 14, p. 513.

CHAPTER XVI

SOME RESULTS RECORDED HITHERTO

IN the present chapter I propose to note very briefly some of the more important results which have hitherto been recorded, and which are not discussed elsewhere. The whole of the German results, for instance, are dealt with in another chapter. It is to be expected that the professional reader who is seriously interested will avail himself of the references here given, and I shall make no attempt to deal with these results exhaustively.

Adhering approximately to the chronological order, we may begin with Dr. Beard's mouse experiments. The reference here is the *British Medical Journal*, p. 140, Jan. 20, 1906, where will be found a brief paper by Dr. Beard, entitled "The Action of Trypsin upon the Living Cells of Jensen's Mouse-tumor." It was this remarkable paper that first directed my active attention to the subject of Dr. Beard's investigations, but it is of interest to observe that he himself undertook the experiments merely in order to direct the eyes of surgeons and pathologists to his earlier and more fundamental work, and regarded the result as a matter of course. In the articles which I wrote in the United States, and which led to action there, I laid much stress upon the findings in the mouse—but these are now of historical rather than immediate interest.

"Jensen's mouse-tumor" took its origin in a mouse

about four years ago, and has since been the subject of exhaustive study by Prof. Jensen, of Copenhagen, a most distinguished worker in this field. It has been transplanted into some thousands of mice, the majority of which it has killed. Under Dr. Beard's direction, several mice were inoculated with tissue from this tumor, in November, 1905, and after about five weeks, when seven or eight mice had developed well-marked tumors, two were made the subject of trypsin injections. The remaining mice with tumors were observed for comparison—or, as we say, were used as "controls." I will quote Dr. Beard's own description of the results:

"After ten days, when four injections in all had been made into each mouse, one of them was found dead by the laboratory servant. The post-mortem examination made by Dr. Wade revealed no cause of death. But for the presence of a tumor mass the mouse appeared to be quite healthy. The laboratory attendant thought that it had got caught between the cage and food vessel, and so (when intoxicated) had caused its own death. The microscopical examination demonstrated that every single cell of the tumor was in degeneration, fully half of them being represented by shapeless masses of particles, probably remains of nuclei, and all the rest were mere skeletons of cells. Even these seemed in very many cases to be crumbling and falling rapidly away, as though in a hurry to quit the scene. The somatic tissues of this mouse, as represented by the leucocytes (white blood-cells) and connective-tissue stroma cells, were quite normal, and in the following instance also. The treatment of the second mouse lasted for twenty-two days, when it was killed, since on that day one of the untreated mice died of its tumor. In the case of that mouse the tumor

was as large as the last segment of a man's thumb, while in the treated mouse it was only as big as a lentil. Microscopically, this latter apology for a tumor was in advanced degeneration, shrinking away to nothingness, and quite harmless. . . . Even without further treatment the tumor would have, in all probability, been absorbed shortly, or its remains cast out."

Dr. Beard's results were confirmed by Dr. G. Zanoni, who is the Director of the Instituto Therapeutico Italiano, at Milan (*Gazzetta degli ospedali e delle cliniche*, March 18, 1906). As the whole world was made aware through the mouth of H. R. H. the Prince of Wales, the Imperial Cancer Research Fund has failed to obtain these results. I write in October, and hitherto no notice whatever has been taken of Dr. Beard's challenge in *Nature* (Jan. 10, 1907) that the details of these experiments should be published. At present the publication of these results, without the evidence for them, constitutes interesting information about the Imperial Cancer Research Fund, but none about cancer.

I briefly note also that Dr. Odier, of Geneva, appears to have controlled cancers in animals by the use of pancreatic ferments (*La Semaine Médicale*, Feb. 28, 1906; *La Presse Médicale*, June 30, 1906).

We pass now to malignant disease in man.

The first important case was published by Dr. Clarence Rice, of New York (*New York Medical Record*, Nov. 24, 1906, p. 812). This is a case of what cannot be doubted to have been cancer of the voice-box, or larynx, and it was reported cured. Results definitely followed the use of trypsin, and in proportion to the dose. Dr. Rice and his fellow-worker remark that only one cause for doubt as to the malignant nature of the growth existed,

and that was the unprecedented fact of its cure by these means. That, however, is no longer an argument. Says Dr. Rice: "The results obtained left no ground for doubt that this treatment exerted a very prompt action upon the growth." I hear (October, 1907) that this patient is now quite well.

The next paper published was the report of Prof. Morton (*New York Medical Record*, Dec. 8, 1906, p. 893). This paper is substantial and authoritative: it deals with twenty-nine cases and the work of eight months. Though during the whole of this period, as I am now convinced, Prof. Morton was using doses far too small, he had most remarkable results. Certainly his report is the most amazing reading. In order to show the reader the quality of his results, I here quote the greater part of his summary:

"*Comments upon above cases.*—1. Two of them, cases 10 and 14, severe cases of face cancer, are cured to date by the use of trypsin. . . .

"3. In all cases signs of amelioration in the progress of the disease have been observed.

"4. Cases 1, 2, 3, 4, and 8, as well as others not specially recorded among the hospital cases, demonstrate that trypsin produced constitutional reaction characterized by rigors, shivering fits, fever, pain in the back, sense of weakness, drowsiness, etc., but of temporary duration.

"5. Cases 1, 2, 3, and 11, among others, demonstrate beyond question that trypsin may produce local reaction in a cancerous tumor, indicated by swelling, heat, pain, or increased discharge.

"6. Cases 20 and 21 demonstrate that enlarged glands associated with cancer have rapidly diminished in size under the influence of trypsin.

"7. It has already been pointed out that these cases were mostly absolutely hopeless at the time of beginning treatment.

"8. Rigors and increased temperature following within a few hours the injection of trypsin, is an encouraging sign, since it indicates that the cancer has been attacked by the trypsin. The toxic action is due to the toxic action of absorbed and destroyed cancer products.

"9. Trypsin has a decided effect in reducing cancer cachexia (system-poisoning) and in improving the general health.

"10. Trypsin, in many instances, as notably in cases 12, 13, and others, demonstrates that even in severe cancer . . . the disease may be brought to a halt, so to speak, even if the patients do not eventually recover.

"11. The use of trypsin has caused hæmorrhages to cease and has alleviated pain.

"12. It is a fact that the patients frequently refer their greatest feeling of improvement to the period of time when they are taking amylopsin following trypsin. An important, as well as a difficult, feature of the treatment, therefore, is to reasonably determine the proper time to administer the diastatic ferment as well as the requisite amount, following or during the use of the trypsin. It has seemed to me that the pure diastase (*injectio-amylopsini*) had much to do with favorable results."

Prof. Morton came to an unduly optimistic conclusion regarding one of his cases, which was unfavorably reported upon some time later, arousing in various hostile quarters a chorus of the most malignant delight. One class of our critics have exposed their motives in a highly significant fashion. It can scarcely be a matter of satisfaction that some one has not been cured or has

died of cancer; it can scarcely be a matter of satisfaction to any one, seeing that it may be his turn next, that evidence should be adduced against the existence of a remedy for cancer. When, therefore, a writer fails, as the writer in the *British Medical Journal* has consistently failed, to conceal the pleasure which every piece, or supposed piece, of adverse evidence affords him, it is a matter of the simplest psychological inference to realize that his motives are personal, and not only personal, but so powerful as actually to overshadow the natural desire which every one must possess to find that cancer is within reach of human conquest. It is the unpleasing but inevitable inference from a host of articles which any one with nothing better to do may now refer to, that there exist persons in whom the emotion of joy that some one else has not discovered a remedy for cancer outweighs all other considerations. If it could have been arranged that the treatment, from the first, should be discussed only by experts who themselves happened to have cancer, we should no longer be at the present stage to-day. This is a digression, but it is of general psychological interest.

Prof. Morton reported a further case in the *New York Medical Journal*, March 9, 1907; two operations had been performed, and the patient returned in September, 1906, with a new small nodule situated beneath the chin. This was treated for only ten days, and entirely disappeared, nor was there any return of it three months later when the case was reported.

In the *Journal of the American Medical Association*, December 15, 1906, Dr. Wiggin reports a case of sarcomatous tumor of the tongue, the diagnosis being well confirmed, which was treated and cured by trypsin and amylopsin. The patient was independently examined by

two doctors eight months after the cessation of treatment, I may note, and no trace of the disease could be found. The next American case that may be referred to is that recorded by Prof. J. T. Campbell, of Chicago, in the *Journal of the American Medical Association*, January 19, 1907. In this case, at the time of recording, the cure of a cancer of the tonsil and tongue was almost completed.

Dr. Beard himself gave a brief preliminary report of a further case in his article, "The Scientific Criterion of a Malignant Tumor" (*New York Medical Record*, Jan. 5, p. 24). In this case a lady living in Naples, and suffering from inoperable cancer of the tongue, was treated under the care of four distinguished Italian doctors. So far back as September, 1906, the last remains of the growth came away, and Dr. Guarracino, a prominent hospital physician of Naples, wrote to Dr. Beard, saying: "This is a wonderful result, and I declare that it seems to me the most considerable fact which our science has ever obtained." I write in October, 1907, and I hear that the patient is now entirely free from the disease.

The reader may next be referred to a long article by Dr. Luther of the University of Pennsylvania (*New York Medical Journal*, Feb. 23, 1907), who has made more than five hundred injections and has excellent results to report. Dr. Luther is guilty of no fulsome courtesy toward myself, but if any one will work fairly at this question he is heartily welcome to say what he likes about me.

Dr. Cleaves' article (*New York Medical Record*, June 11) is elsewhere referred to. Here I may merely note that she had several substantial results to report, following upon her letter of nearly six months before.

Still keeping to the United States, we must note the case of Dr. Doran, also of New York, who reports in the *New York Medical Record*, July 6, 1907, a case of sarcoma, a terribly malignant tumor, in which the patient underwent the pancreatic treatment for recurrence of the disease after a most radical and extensive operation. The treatment was begun in the first week of January, 1907, and since April had been very largely relaxed, though not discontinued. The patient had gained twenty-two pounds, and scarcely anything whatever could be discovered, at the time of reporting, remaining from the recurrent growths. Here is a case where surgery had done its utmost, and where nothing else in the whole armory of science hitherto could have availed the patient.

Thirdly, I may refer with equal brevity to a case no less remarkable, reported in the *New Orleans Medical and Surgical Journal*, July, 1907. In this case a cancer of the voice-box or larynx had been excised by the knife, but recurred. The pancreatic treatment was employed for about five months, at the end of which time no disease could be found—nor two months after the treatment was discontinued.

If now we turn to Great Britain, the record will be found absolutely in accordance with what any student of history and human nature might have predicted. From Edinburgh, for instance, where Dr. Beard works, there is no word whatsoever of any achievement, or, indeed, of any result at all. I ask for proper detailed records of failure wherever obtained. It would be obviously false to say that they will be as welcome as records of success, yet it is quite possible that they may be far more valuable. Edinburgh, that great center of medical science, has nothing to say for or against the ferment treatment, and

I recall the historical facts which attended the pioneer labors of Simpson and Lister in that city.

For records of substantial success in Great Britain we had to wait until a few days after the publication of my article in the *Contemporary Review*, in which, after recording results in Germany and America, I had scarcely more to say as regards Great Britain than that results would be published in a few weeks. On August 31, 1907, the *British Medical Journal*, which had refused to publish Dr. Cavanagh's report, later noted, published a brief memorandum by Dr. Cutfield, which may be noted as the first of its kind in that journal. The patient had been operated upon at Guy's Hospital for an abdominal tumor, rapidly growing, which the surgeon was unable to remove, and which had already given rise to various secondary growths seen at the operation. The treatment was begun on the 1st of May, under Dr. Beard's directions, at which time "the whole epigastrium appeared to be full of solid tumor. He was, besides, wasting rapidly, and had become extremely weak; suffered a great deal of pain, especially in the back; had nausea and vomiting, pain after food, and sleepless nights." Dr. Cutfield continues as follows: "Very soon improvement set in, and continued steadily. First, the vomiting, nausea, and flatulence disappeared, and the appetite improved, and then gradually the pain lessened, and the swelling also steadily diminished, while the weight, which was recorded weekly, regularly increased. The injections were continued daily for three months, and at the end of that time the man was practically well, the only symptoms left being some abdominal discomfort, and, occasionally, pain. He eats and sleeps well, and attends to his business regularly; his weight is only a few pounds less than it has been for

many years, and the only thing to be felt in the abdomen is some hardness in the line of the incision, and a little to the left of it the remains, I suppose, of the cyst which was left stitched to the abdominal wall. I do not say that he is cured, but no one who has seen him can doubt the immense improvement that has taken place, and, considering how rapidly he was deteriorating before treatment commenced, and how promptly and steadily the improvement took place after the treatment began, it is extremely difficult to believe that the trypsin was not the cause of that improvement."

For reports much more extensive, however, we must turn to the *General Practitioner*, which (June 15, 1907) had already discussed the significance of my articles in the *Daily Mail* in its editorial, which may be heartily commended as a rare example of open-mindedness and judgment. I only wish I had space to quote it in full. On August 31, 1907, this journal published a preliminary report "On the Pancreatic Treatment of Cancer," by Dr. Henry Meggitt, who has been practicing the treatment since December, 1906 (having begun it the day after the appearance of my *Pall Mall Gazette* article), and under my eyes since January, and who records the results hitherto obtained in six cases, of which four had previously been the subject of extensive surgical operation at very skilful and well-known hands. All these patients were admittedly past all surgery, and in them—as indeed in the other two—the nature and the high activity of the disease, on coming under treatment, was utterly beyond the vestige of question. The professional reader must be referred to that report. I may quote a word or two here from the general remarks included. "In all cases I have seen I have not yet met with one that has not obtained

benefit. Trypsin has absolutely done away with morphia. The patients eat better, they feel better and happier, and put on weight. As a general practitioner of fifteen years, I look back with horror to the old days of treatment, when nothing was done but injections of morphia, and the sooner the patient was dead, and out of his pain and misery, the better for everybody. . . . Trypsin will, I am confident, if intelligently injected, relieve all pains of cancer, it will quickly remove all fœtor and discharge from broken-down growths when applied both locally and hypodermically. By the end of two months' injections marked improvement in glands will be noticed; they become smaller and softer. The size and hardness of the tumor itself at the same time shows marked shrinking. The general health improves in what I can only describe as a startling way. Cachexia disappears entirely, weight is put on, the appetite is good, and, as there is never any pain, the patients sleep well."

In the *General Practitioner* for the following week, September 7, 1907, there was published the report of Dr. Francis Cavanagh's two cases which the *British Medical Journal* refused to publish. The first patient had had a cancer of the stomach for two or three years, with all its typical accompaniments—pain, sleeplessness, cachexia, and emaciation, and with large and hard glands in the groin. The patient's weight on coming under treatment was 6 stone 10 lbs.; the general condition was such that the operation recommended by a consultant could not be performed. The patient said that her pain had been practically continuous for over a year, and it prevented her from ever sleeping for more than one hour at a time. Dr. Cavanagh says:

"Within a week of beginning injections, pain was re-

lieved to the extent of allowing the patient to sleep for six consecutive hours. For over sixteen weeks now the pain has totally disappeared, sleep is perfectly normal, appetite greatly improved, the cachectic skin has become quite healthy-looking, the tumor has decreased to half its original size, the glands are much smaller and softer, and the patient has gained pounds in weight. . . . The cessation of pain and the improvement in this patient dated from the beginning of Dr. Beard's treatment, and this treatment was the only factor that was superadded to the patient's previous mode of life."

In the second case an abdominal operation had already been performed, and showed "a most extraordinary cancerous and irremovable condition." A palliative short-circuit (gastro-enterostomy) was made. A fortnight later the patient was attacked with most severe pain, "at first related to meals, then more continuous, till at last it persisted without cessation for three weeks, and her nights were spent writhing in agony on the floor. Morphine said to be useless; certainly repeated thirty minim doses of tr. opii were ineffectual. . . . The patient was injected with trypsin at a time when she was still in that pain, which had lasted for three weeks. The pain disappeared that day. . . . Three days from the first injection had an attack of pain for two hours, then was quite free for six weeks. . . . The attacks of pain still occur, but they are readily overcome, and she sleeps well every night. . . . It cannot be expected that this patient will survive, though she is now quite able to go about; it is certain, however, that she would have been dead before now but for trypsin and amylopsin."

These are the cases which the *British Medical Journal* refused to publish in circumstances which I detail else-

where. I submit the fact to the judgment of public and professional opinion. I agree that, as the journal said in refusing them, they are "incomplete." But I will observe that the object of this treatment is not to convince anybody of anything, but to help the otherwise helpless. In my judgment, which I believe universal opinion will sustain, the refusal to publish these cases, after a failure to acknowledge their receipt for three weeks, and then only on Dr. Cavanagh's inquiry, is disgraceful.

In the same issue, the *General Practitioner* devoted its leading article to this subject, and thus describes the conclusion at which it has arrived: "This conclusion is, without at this moment considering the possibility of ultimate cure, that the action of trypsin and amylopsin, when properly administered, is undoubtedly in the direction of ameliorating the more distressing accompaniments of cancerous disease, most notably the pain. On such grounds alone, therefore, the method would be amply justified." The journal goes on to note that the observers at the Middlesex Hospital "invalidated their own report on this question by self-convicting themselves of faulty technique. If there is one point that is insisted on, not only by our own contributors, but by the German investigators, it is that necrosis and suppuration should never occur at the seat of injection. Yet this very fault caused by the administrator is one which the Middlesex Hospital has urged against the method!" In a letter to the *General Practitioner* of the following week, Dr. Dickinson pointed the moral, concluding his letter thus: "Probably the inflammatory process set up by septic injections destroys the ferment and nullifies the treatment. Thus the profession and the public are being misled." This comment upon the Middlesex Hospital report, I may remark, ex-

ceedingly obvious and radical though it be, is the first that has anywhere appeared, apart from Dr. Beard's and my own communications "in the lay press."

The editorial writer goes on to observe that in my *Contemporary Review* article I was unable to quote evidence from English sources, and in the following sentences reasserts the contention which I put forth in the *Observer*: "For this, in our opinion, the *British Medical Journal*, on account of the attitude assumed by it in the beginning, is largely responsible. The busy doctor has not time of himself to read even the original articles regarding discoveries or theories, much less to reinvestigate their bases, so that his medical journal has a great responsibility, since to it he naturally turns in his desire to keep up-to-date. What his journal condemns must naturally affect his own opinion, and the condemnation of trypsin has been much more than tacit."

It will be readily understood that the *British Medical Journal*, which found itself unable to reply to my *Observer* indictment, later to be noted, has made no answer to this.

Some general remarks fall to be made here. In the first place, the reader will not confuse the statement of these results with any assertion as to their ultimate significance. It is indisputably right that they should be stated. They prove abundantly, I hold, that beneficial results have been obtained by the ferment treatment. On the other hand, from my own point of view, it would really be far more profitable to discuss the details of failures, with the object of ascertaining their cause. It is much to be regretted that properly reported records of failure are as yet nowhere to be found, so far as I know; records such as that of the Middlesex Hospital, which

tell us nothing as to the urine, let alone the blood, of the patients, and which issue in the warning against local disasters, for which there exists absolutely no excuse—are of small profit. If, on the other hand, we had records of cases in which the treatment was applied in adequate and cleanly fashion, but without good results, these of course would be of the utmost value in helping us to form an estimate of the range of application of the new treatment. If some of its advocates should be inclined to form an unduly favorable estimate of its applicability, they are fully entitled to point out that their judgment has necessarily been affected by the absence of recorded failure where the treatment has been properly applied. If by chance such failure cannot be recorded, except, as is very probable, in cases of which the malignancy has been factitiously enhanced by surgical or other irritation, then so much the better.

Certain of the cases above recorded purport to be cases of cure; but I wish to insist as plainly as I can that, if no case of cure nor of anything resembling cure had been reported or was ever to be expected, the beneficial results of the treatment would still entitle us to claim for it a universal place in the treatment of cancer. If it will give ease for agony, sleep for sleeplessness, sweetness for fœtor, even without postponing death for a single hour—even so it will be, on the whole, immeasurably the greatest boon that science has yet offered to the cancer patient. To refuse to relieve pain because you are not sure that you can cure the disease, is a wholly imbecile and brutal proceeding, which is countenanced in no other case, and the advocacy of which I think no one could have anticipated before this question was raised. The introduction of nitrites was the greatest step ever taken

in the treatment of *angina pectoris*; the introduction of digitalis the greatest step ever taken in the treatment of heart-disease. These drugs are universally used and applauded, and are of immense service to mankind. Neither of them is in any sense whatever curative. Let all the records of cure, or apparent cure, or approach towards cure in this chapter be wholly discredited: even then the control of the distressing symptoms of cancer by the ferments entitles them to rank in the treatment of this disease as wholly on a par with digitalis in heart-disease, or the most valuable known remedies so-called in the treatment of all other diseases except those very few for which curative remedies exist. If this book were written solely in advocacy of a remedy for the pain of cancer superior to morphine, and if that sole claim were to be upheld, the volume would have far more than justified its appearance, and every criticism it contains of those who have opposed the treatment.

In passing these sheets for the press, I take the opportunity of noting what constitutes the report of the tenth case published in Great Britain since my *Contemporary Review* article. This is to be found in the *Medical Press and Circular*, October 2, 1907, so that favorable results have now been recorded, though without comment, by the two bitterest opponents of the treatment in the medical press in this country. The doctor says, "Without exaggeration, I can describe the results as marvelous." After two months' treatment the case passed into other hands, Dr. Matthew's successor having "no faith in trypsin." The treatment was discontinued and the man died six months afterwards of "exhaustion," having had no pain or hemorrhage. I do not doubt that this was poisoning by the products of the dead tumor, which the use of

amylopsin would in all probability have averted. In this case (cancer of the tongue) the treatment, until its discontinuance, did everything that could be asked for, nor were there any local troubles at the site of injection—in fact, nothing but the best results.

CHAPTER XVII

THE CLAIMS OF THE TREATMENT

IT has been part of the method of our opponents to assert that I have declared trypsin to be an infallible cure for cancer, always annihilating the disease. It need hardly be said that references are never given. No one has at any time made such claims, and those I make for the treatment now, after the experience of a host of observers during nearly three years in all, are, if anything, greater than I have anywhere made, or any one, so far as I know, has anywhere made, hitherto.

That trypsin and probably various other ferments have a specific toxic action upon the cells of malignant tissue in general, whether carcinomatous or sarcomatous, is now a fact repeatedly proved, as to the specific digestion both of dead malignant tissue in a test-tube, and of the living tissue in its site of growth; that is to say, both *in vitro* and *in vivo*. This has been repeatedly proved by independent observers of the highest repute in Berlin alone during the past two years; and, as a fact, is, like other facts, independent of any theory whatsoever. It does not depend upon, nor does it demonstrate the truth of, the trophoblastic theory of cancer; and it does not prove that trypsin, for instance, is of use in the treatment of the disease, since, for instance, it might be that the products of its action upon cancer in life were far more deadly than the cancer itself. It is merely a fact—that a

ferment or ferments are known which, *in vivo* or *in vitro*, have a specific digestive action upon malignant tissue. It will be evident to the scientific reader that the indication of this by Dr. Beard, on December 13, 1904, was an epoch in the study of the disease, whether his trophoblast theory be right or wrong, and whether or not we of the present generation can turn the cancrotoxic ferments to practical account. No one will question that, if all the rest does not now follow, it will follow. The enemy's weak point has at last been found, and if we do not strike home, our descendants will. The conquest of cancer must be, at the very least, within hailing distance, the naturally appointed weapons being at last in our hands.

But, as every one knows, more is claimed than this, and I only insist upon it as a demonstrated fact—which, so far as the test-tube experiment, at any rate, is concerned, any one may prove for himself—because in Great Britain the fact is not yet admitted, the foreign evidence having been ignored, and the official native observers having failed and having loudly advertised, with the aid of royal lips, their failure to record it; forgetful that in any scientific experiment failure only proves that the particular observer has failed.

I have more to say, however, than that we have at last found the right road to our goal, and the present question is as to what Dr. Beard's discovery is worth to us to-day.

In passing, I claim what no one will dispute, and what was known, though not acted upon, even before Dr. Beard began his researches twenty years ago. It is that trypsin, the most powerful of all known proteolytic ferments, can digest, at the temperature of the body, many forms of dead proteid tissue of animal origin. On this

unquestioned ground I commend its local application in all cases where a cancer or other malignant tumor is exposed to the air, and undergoing necrosis or local death upon its surface. Properly applied in such cases, trypsin will invariably keep the surface perfectly clean, affording bacteria no dead material on which to grow. In consequence it will effect what any agent would effect by such action: it will abolish all malodorousness, such as is the curse of most advanced cancer cases, and it will prevent that absorption of bacterial poisons to which, in part, at least, the constitutional poisoning, or so-called "cachexia," of cancer is due, together with the loss of weight which is its consequence. Familiar examples are cancer of the mouth, cancer of the uterus, and exposed cancer of the breast. I ask the surgeons, believing nothing whatever in this book except that trypsin is a proteolytic ferment, and probably the most powerful of its kind—certainly the most powerful of animal origin—to employ it for this purpose. Let them use it solely as a local wash, and I predict that, having abolished the patient's cachexia and the foetor of the disease, they will find reason to apply it also remedially, in the full sense. The local application alone cannot be remedial, except possibly in superficial cases of rodent ulcer without secondary growths. For this method, the use of which alone would constitute a great advance in the treatment of cancer, I claim further a specific advantage over the employment of iodoform, formalin, carbolic acid or other antiseptics. This is that, according to Von Leyden's law, these agents, in so far as they reach the living cells of the growth, stimulate such as they do not actually kill; while trypsin, as he has shown, is unique among chemical agents, and resembles ethereal radiations of short-wave length, such as the Röntgen

rays, and the ethereal radiations of radio-active substances, in that it causes no increased growth and no enhanced malignancy in the tumor. I further ask the countless surgeons and others who have hitherto declined to employ trypsin for this purpose, on what grounds they have so declined? Do they deny that trypsin can digest dead proteid tissue, or are they perfectly satisfied with their present methods of dealing with the smell and the bacterial poisoning of exposed cancer, or do they attribute to the local use of trypsin some dangers of its own? Or are there graver explanations?

I claim, in proceeding, that the new treatment, properly applied, is absolutely free from all danger, and in this respect I claim for it a unique place in comparison with surgical operation, the use of caustics or the Röntgen rays or radio-active substances. It has been clearly shown—what scarcely needed showing—that trypsin, a normal inhabitant of the body, produces, even in enormous doses, no symptoms whatever but increase of weight in healthy animals, healthy human beings, or patients suffering from innocent tumors.

The injections may be so made as to cause abscesses. In not far short of two years I have never seen this result, and some individual workers have given as many as a thousand injections without once obtaining it. The accident may befall any one, but he to whom it occurs frequently is not suited for the practice of medicine, and him only would I warn against the treatment.

There are remoter and less inexcusable possibilities, however. Drs. Pinkuss and Pinkus have shown, in their paper in *Medizinische Klinik*, that injections made deliberately in animals, from pancreas-glands that were not fresh, caused symptoms of serious poisoning. I here as-

sume that the injections are made as described in the chapter devoted to that subject.

Even then, in cancerous patients, and in them alone, injections made in cleanly fashion may cause constitutional symptoms. I note in passing that these are an index and proof of the action of the remedy upon the disease. They may be met by the use of amylopsin, the adjuvant value of which is attested by observers both in America and Germany—and now even in Great Britain. No case has been reported in which the new treatment, properly applied, without abscess formation, has proved dangerous or even injurious to the patient. It need hardly be said that, if patients were occasionally killed by it, the treatment would be condemned by all and not least by the surgeons, though patients unfortunately die every day from, and under, operations for cancer. To a new treatment canons are applied which no one dreams of applying to an established treatment. But in respect of risk to life no credible treatment of cancer hitherto proposed can vie with the pancreatic treatment.

I claim that, in addition to removing all fœtor and preventing bacterial intoxication or cachexia otherwise caused, the new treatment is a specific for the pain of cancer. I have never seen morphine injected, or asked for, or required by patients undergoing the pancreatic treatment. Without any of the grave and obvious disadvantages of morphine, it accomplishes in this respect all that morphine ever accomplishes, and habitually succeeds where morphine fails. There is no longer any need for any cancerous patient to become a morphino-maniac. Says Dr. Cleaves (*N. Y. Medical Record*, June 1, 1907): "The indications are that the use of the enzyme (ferment) treatment will have to be continued over long

periods of time and perhaps at intervals throughout life, but as the absence of pain is a constant accompaniment, it would seem logical and better to have a patient with the trypsin necessity rather than the morphine habit." This is the evidence of nearly a year's experience with several cases. Prof. Morton, after eight months' experience in twenty-nine cases, reported: "Relief of pain in all cases"; and cancer, as I have known it since February, 1906, is a disease in which (cancerous) pain—like foëtor—does not occur. Dr. Pinkuss in Germany and Drs. Meggitt and Cavanagh at home have lately reported similarly.

We know the influence of the mind over the body, we know that violet leaves may abolish the pain of cancer—or Christian Science, or injections of salt and water called morphine. The reader may assume that the relief of pain by trypsin is of this order. From the first I have assumed that the critics would so assume, and therefore I have directed little attention to the fact, beneficent and constant though it be—in my experience and that of many others. The skeptic is welcome to make the same assumption still; only I ask him, when and if other means fail to relieve pain, to try trypsin. He will not go back to morphine. In short, there is claimed for trypsin, properly used, the supersession of morphine and other analgesics in the treatment of cancer at all stages. A theory of its action is not essential and may be premature; we do not cease to employ morphine because its action cannot be explained; but the remarkable consistency of the result, whatever the facts of the case in question, and the success of trypsin in abolishing pain and permitting sleep, even where the largest possible doses of morphine fail, make it probable, I think, that the **action**

is not an anæsthetic one, either by the direct action of the ferment on the sensorium or the nerve-endings, or by the action of its digestive products; but is due to its arrest of the growth of the tumor at its margins, and to the lowering of its pressure by reduction of its density. It is generally recognized that the pain of cancer, like its constitutional poisoning, and indeed its symptoms in general, is, so to speak, accidental. The tumor is not supposed to secrete substances which irritate the nerve-ends, but is supposed to cause pain solely by pressure. There are, of course, no nerves or nervous elements evolved in any malignant tumor. Pain is not an early symptom of cancer, and many fatal cancers are painless throughout.

It is claimed for the treatment, then, that it is an unapproached, constant, and wholly effective remedy for the pain of cancer. I do not for a moment believe that it would have any effect—except through the mind—upon any other pain; and if any one asserts that its action in cancer is through the mind I will not concern myself to contradict him. In fact, I will assent, if the assent will encourage him to make promises to the patient, and so utilize his mind as far as possible. I do not assert how it acts, but simply that it does act.

Though the relief of pain has hitherto been observed by every one who has made competent trial of the new method, though I have never seen it fail in this respect, and though even Prof. Bier, employing ferments by means of the injection of blood, obtained the same result in nearly all cases, it is, of course, possible that a nerve may become involved in a growth, without being destroyed, in such a fashion that even the instantaneous death of the growth would not relieve pain; and it is even conceivable that, in the course of its shrinkage or replace-

ment by fibrous tissue, a tumor might press upon an undestroyed nerve even more painfully than before. In such cases the treatment would fail to relieve pain, and pain might conceivably become an increasingly prominent symptom for some time, even during the actual cure of the disease. These possibilities must be remembered, though at the present time they remain possibilities only. In such cases it is quite conceivable that morphine would succeed where trypsin failed to relieve pain, though possibly curing or arresting the disease.

The discovery of a remedy which prevents, abolishes, or, at the very least, arrests the progressive cachexia of cancer, abolishes the smell of exposed cancers, and relieves the pain of all cancers, without risk and without stimulation of the growth, would abundantly warrant us in giving it the earliest and widest publicity; but much more is claimed, though I submit that these claims alone should insure for it the widest trial, and that more—if more there be—might then be allowed to appear for itself.

It is not claimed for this remedy, nor has it ever been claimed by Dr. Beard or myself, nor can it ever be warrantably claimed for any remedy yet in the womb of Time, that it will keep alive indefinitely any and every cancerous patient. In a large proportion of the cases under trial hitherto, the patient was already, on coming under treatment, a broken or even a moribund man, worn out and dismembered by repeated operations.¹ These had greatly enhanced the malignancy of the growth, according to the general rule of the irritation of cancer by the knife or other agents. Already the disease and the knife had

¹Many patients have died before the preparations could even reach the hands of the physician.

attacked and destroyed various tissues and organs, blood-vessels, nerves necessary to local health, and so forth. No human or natural power, nothing but a supernatural interference, could restore what had thus or otherwise been destroyed. Cut the skin to-day, and though it heals to-morrow, certain glands and cells characteristic of skin have been destroyed once and forever. Trypsin has added months to the lives of such patients; it may in some cases have averted death indefinitely; but it cannot alter the past. It cannot re-create destroyed structures, it cannot restore a ruined constitution, it cannot replace by healthy kidneys those already poisoned by the passage through them, for months or years, of bacterial poisons.

To this the reader may reply that no one but a fool would expect trypsin to work miracles. This I grant, and thank him for the word; for now we know how to describe those who have demanded that trypsin shall perform these miracles and perform them every time, and who, with joy shamelessly unconcealed, have hailed as demonstration of its worthlessness the deaths of such patients, without asking whether life was not prolonged or whether the patients' latter days were not incalculably ameliorated by the treatment.

The pathological evidence elsewhere cited strongly suggests that it would be well to make no claims whatever—except as to the *relatively* minor matters already discussed—for the pancreatic ferments in cases where the malignancy of the disease has been indefinitely increased, not to mention the mutilation of parts, by surgical operation, and especially by repeated operation. Here, again, a grossly unfair and illogical criterion is applied. The test case for surgery shall be the earliest possible case, chosen by the surgeon, and free from secondary growths. The

test case for trypsin shall be this same case, chosen by the surgeon again, months or years later, after one or many surgical failures, when the liver and other internal organs are affected by secondary growths, and the patient's excretory and digestive organs are irremediably ruined by bacterial poisoning.

This is not the fault of the surgeons, but of human nature. If trypsin were the orthodox remedy for cancer, and some one proposed the knife, the orthodox would hand over their moribund cases, if such there were, to the innovator, and condemn him because he could not save every one without exception. I have seen trypsin perform most things short of a miracle, but no miracles yet. It is not a creator; but is the knife?

Let us revert for a moment to the theory. As Dr. Beard has put it to me, when nature kills and digests normal trophoblast—the “syncytium” or mantle-tissue of the chorion—in normal pregnancy, by means, as he asserts, of the trypsin produced by the foetal pancreas, she has only given it a seven weeks' start; and no surgical operations have previously been performed, heightening its malignancy—for undoubtedly it is a malignant tissue, so long as it lives, in its action on the wall of the womb. Now nature never fails in this respect, provided that the foetal pancreas has due opportunities for action. Otherwise, as we know, chorio-epithelioma, or “trophoblastoma,” as it should be called, is apt to develop; perhaps it invariably develops if the foetal pancreas, say before a miscarriage, has not already killed it. Now, assuming the relevance of these facts to the case of cancer or “irresponsible trophoblast,” we may argue that the nearest possible reproduction of the natural conditions would be the use of trypsin in early cases, unmodified by the knife or by caus-

tics. Whether they are accessible or not to the knife or other means, they are never inaccessible to the blood, which will convey the ferment to them.

It is not claimed, then, that trypsin will cure outright all such cases as the surgeons, after one or more operations, have abandoned. I certainly believe that the ferment treatment should be employed in such cases, as in all cases, and that it will prolong life, relieve pain, abolish fœtor, and at least retard the disease. It may even kill the tumor outright, but fail to save the patient, who dies as the gradual consequence of all that he has previously undergone. As for the critic who argues that if trypsin cannot save these patients it is condemned, and that there is no treatment for cancer but the knife—I will waste no further words upon him.

But, quite apart from the factitious enhancement of the malignancy of a growth by the knife or caustics, or the use of antiseptics, we have to recognize that different tumors vary widely in their degree of malignancy, though all may be unmistakably malignant. The causes of these differences have been practically or wholly unexamined hitherto. The pathologists, unaware that the problem of cancer is a chemical one, have confined themselves to the association of certain microscopic characters with this or that degree of malignancy.

But a moment's thought shows that the shapes of cells are not the cardinal matter here. The malignancy of any tumor is determined, I submit, by the ratio between the amount and potency of the ferment produced by it on the one hand, and the amount and potency of the antidotal substances of the blood and normal tissues on the other hand. Thus it is a common experience to find the malignancy of a tumor reduced, and its growth retarded,

by the administration of the antidotal substance, trypsin, which alters this ratio in favor of the host as against the parasite.

But in general, it may be argued, I believe, that the dominating factor in this ratio is the factor of the cancer ferment or ferments; and an argument in favor of this supposition is the fact that operation, caustics, etc., so constantly enhance the malignancy of a tumor (which alters meanwhile in microscopic structure). In such cases the patient's body is approximately the same; it is the tumor that has been modified.

Hence, on the whole, the malignancy of a tumor depends on the amount and potency of the ferment or ferments produced by it. Eugen Petry, in 1899, identified a cancer-ferment, which Dr. Beard has named "malignin." That such a ferment exists is a matter not of observation but of obvious necessity. But there is no warrant for asserting that there is only one cancer-ferment. There may be, for instance, almost as many as there are different degrees of malignancy. Is it not more than probable that the ferment produced by a scirrhus of the breast, which lasts for twenty years, is very different from the ferment of a melano-sarcoma which kills in as many weeks? The difference may well be as great as, or greater than, the difference between the digestive potency of trypsin or amylopsin on the one hand, and pepsin or the ptyalin of the saliva on the other hand.

It is quite conceivable that, for instance, certain highly malignant sarcomas may produce ferments which trypsin cannot neutralize, but which actually digest it. There is already evidence to show that in such cases much larger doses of trypsin are necessary in order even to arrest, let alone kill, the tumor. There may be cases which, from

the first, unmodified by the knife or by caustics, are incapable of arrest by trypsin. It is, therefore, not claimed—at present, at any rate—that, even in the most favorable circumstances, trypsin would cure all cases of malignant disease. But the ferments of cancer-cells are intracellular, and it is scarcely possible to imagine that any intracellular ferment can, during life, be as potent as the extracellular trypsin.

On the other hand, writing now at the beginning of this subject, and not under the delusion that we are at the end of it, I certainly do not assert that we are in possession of evidence which demonstrates the incurableness from the first of certain forms of tumor by trypsin. So far as I am aware, the pancreatic treatment has not yet been employed in cases of melano-sarcoma or chorio-epithelioma. It has been employed, however, in many cases of sarcoma, and the reader may be referred to the case treated by Dr. Doran (*N. Y. Medical Record*, July 6, 1907). Enormous differences have been observed between the results of treatment; but until the preparations are standardized we have no right to assume any other explanation than that which has undoubtedly been the correct one in most, if not in all cases, hitherto. We may note that relatively non-malignant growths have responded little to the treatment in some cases, while virulent sarcomas have yielded in others. In some, at any rate, of the cases to which I refer, absolutely worthless preparations were employed. Thus I neither assert nor deny that there are primary cases of malignant disease in which trypsin is impotent to destroy living cells—though it will always dispose of the products of superficial necrosis. The German observers, Schütze, Bergell, Pinkuss, and Pinkus, have shown that no anti-trypsin is

formed by the healthy body when trypsin is formed into the blood. But I regard it as a possibility, if no more, that when trypsin is brought into action against cancer, the cancerous cells may produce an anti-trypsin. Indeed, on general principles, this is perhaps more likely than not. The blood of patients under the treatment should be examined in this regard. The very principles which make intelligible the absence of anti-trypsin formation in the healthy body, and the development of anti-bodies to foreign ferments, would also make intelligible the development of an anti-body by cancer when attacked by what is to it a foreign ferment and a dangerous one. This, of course, is only speculation, so far, but I think it is reasonable speculation, and may be useful.

In the absence, hitherto, of positive evidence on this point, I am much inclined not merely to regard with a new interpretation the cases where absurd doses of trypsin—two per cent. solutions and the like—have been employed, but also to question the propriety of starting the treatment, or any form of ferment treatment, with minute and gradually increased doses, as if one were attempting to establish artificial immunity in a case of hydrophobia. The question arises, I think, *whether this may not be precisely the fashion in which one would proceed if it were being attempted to establish immunity on the part of the tumor.* I believe that I have seen indications which strongly suggest that this establishment of immunity may occur; and if I, myself, were to undergo the treatment, I should prefer to start with very large doses, in the expectation that the object to be aimed at was the death of the tumor before it had had time to establish immunity—assuming such to be possible. This is how the bac-

teria of disease actually kill. They pour such a dose of their ferments or toxins into the blood that death occurs before immunity can be established. If any device can keep the pneumonic patient alive till the tenth day, rather than the sixth, he will probably recover; the object is to tide him over the *crisis*—*i.e.*, to keep him alive until he can immunize himself. It may be suggested that in the attempt to kill a cancer we should adopt the methods only too successfully employed by the microbes of disease—make the initial doses so large that the subject has no time to defend himself.

My personal observation has chiefly been concerned with Messrs. Squire's preparations, which are very rich in amylopsin; and the precautions as to initial dosage, much insisted upon by some workers, are irrelevant with these, and presumably with any in which sufficient amylopsin is contained. A first dose of 1 c.c. of the Standard 11, containing 500 units of tryptic and 200 of amylolytic activity, is perfectly well borne; and if the line of argument here submitted should prove to be valid, it is evident that such doses, or, indeed, the largest compatible with safety, should be given from the first. I doubt whether, in the presence of sufficient amylopsin, there is any upper limit of safety, especially if the kidneys be sound.

Further, if the above argument be valid, it must be found that some patients do well for a time and then cease to advance, or even go back. Assuming such cases to occur, and other explanations failing, I would incline to the view that the growth has become immunized to the ferments, and is recovering, just as the pneumonia or influenza or typhoid patient recovers. Such cases must be prevented from occurring, if possible, by vigorous initial treatment; but if they do occur, plainly the doses of

the ferments must be greatly increased. Perhaps the difference between advanced recurrent cases and early unoperated ones, in respect to ferment treatment, may be reduced to some such terms as will readily suggest themselves to the reader who finds the present argument rational.

Practically the only specific remedies known to medical science hitherto are mercury for syphilis, quinine for malaria, and the antitoxin of Behring and Roux for diphtheria. It is stated, and truly, in general terms, that mercury cures syphilis and quinine malaria; but there are cases of syphilis which mercury does not, and apparently cannot, cure; and exactly the same is true of quinine in malaria. I believe it will be admitted before long that, in the same sense as that in which quinine is said to cure malaria, trypsin and amylopsin cure cancer, in certain cases, at any rate.

The incredible argument has been adduced by some critics, presumably adult, such as the editorial writer in the *British Medical Journal*, and even a writer in *Nature*, that it is improper to speak of a cure of any case of cancer until three years have elapsed without recurrence. I need hardly say that the three years' limit is not a law of nature, and that no possible parallel exists between the degeneration and disappearance of a growth by means of agents carried in the blood and the removal of it by the knife—in which latter case the portions almost invariably left behind usually show their presence within three years.

It is claimed for the treatment that it is applicable to, and should be employed in, all cases of malignant disease, without exception, whether early or late, carcinomatous, sarcomatous, or other, operable or inoperable, operated upon or not operated upon, accessible or inaccessible, sin-

gle or multiple, primary or recurrent, with or without secondary growths, painful or painless, dubious or certain. A large proportion of my correspondence since March, 1906, has consisted of letters asking whether the treatment is applicable to such and such a kind of case. It is more generally applicable than mercury in syphilis, or quinine in malaria. I know of no contra-indication to its use, and no case—or likelihood, or even possibility—of idiosyncrasy to this substance which, be it remembered, is a normal product and inhabitant of the body, and has no action of any kind upon the tissues proper to the body.

I can scarcely do better here than quote from the highly judicial paper of Dr. Cleaves (*N. Y. Medical Record*, June 1, 1907), with the note that I am far from convinced of the truth of the view that the treatment, properly applied, may shorten life. Certainly, Dr. Cleaves herself has not obtained results pointing in this direction, but I believe that she has noted them in other (improperly treated) cases.

The question of the constitutional symptoms following the use of trypsin in cancer has already been discussed. Dr. Cleaves says:—

“Conclusion.—The justification of this treatment is to be found in (1) the pathological findings, (2) relief from pain, (3) absence of odor and necrotic discharge, (4) improved metabolism, (a) in cases that do well, (b) even in those who succumb, (5) increased mental vigor, and (6) by inspiring the patient with hope.

“On the other hand, it may result in shortening life by a few months, but that short span of added existence would be characterized by breaking down of tissues, odor, necrotic discharge, pain, imperfect metabolism, loss of

mental vigor, and by utter hopelessness on the part of patient and friends.

“Treatment should be undertaken early in every instance, and should always be an adjunct to surgical interference in every post-operative case.”

The success and expectations of the treatment are not *fundamentally* affected by the site of the tumor, nor by the existence of secondary growths: in this respect contrasting with surgery. The essential part of the treatment is hypodermic injection, and it is entirely irrelevant to success whether the tumor be of the lip, or the œsophagus, or the liver. The factors of position which determine the success or failure, the applicability or inapplicability, of surgery, are not relevant here. I do not say or suggest that all tumors are alike to trypsin, but that the site of a tumor and the existence of secondary growths are not primary considerations in this connection.

That it is easier to kill a small tumor than a large one, there can be little doubt; but every part of the larger tumor must be directly or indirectly accessible to the blood if it is to live at all—and therefore to trypsin. The factor of malignancy—that is to say, as I suppose, of the potency of the malignant ferment—is the prime factor here, not site or size. This is not to say that it is not a much lengthier process to dispose of the degeneration-products of a large tumor than of a small one, or that the problem of protecting the patient, by means of amylopsin, from these products is not much more pressing in the case of a larger tumor. It is to be supposed, then, that early treatment is to be desired not so much, as in the case of surgery, in order to anticipate the formation of inaccessible secondary growths—all cancer cells being accessible to the blood, or, if not, bound to die of starvation in any

case—but in order to avert the increase of malignancy which usually follows surgical interference, and because the disposal of the degeneration-products of a tumor will be lengthy and difficult in direct proportion to its size.

I do not claim for this treatment that it can be carried out by any practitioner: in this respect it is on a par with antiseptic surgery. There are men who can attend to apparently trivial details, and men who cannot. I am convinced that the *status* of the new method would be very different to-day if none but careful, precise, conscientious and assiduous men had ever undertaken it.

I do not claim for the treatment that it is cheap. It is cheap compared with surgery—very cheap; and perhaps the question of results is relevant here; but it is prolonged, and the injections are not inexpensive, though I, for one, cannot understand how it is possible to turn them out at the present prices.

I do not claim that at present the treatment can be carried out in any part of the Southern Hemisphere, unless very special precautions as to the traveling of the preparations be observed. The Southern Hemisphere will do well to make its own preparations.

I do not claim that the materials for the treatment can be obtained anywhere. In my first articles I said, being anxious to show that the remedy is not proprietary, that trypsin could be obtained anywhere, and did so against the advice of Dr. Beard. I withdraw that statement and, so far as I can now judge, no other that I have hitherto made on this subject.

Of the first importance, I believe, is a theoretical objection which, though long present to my mind in degree, has only lately displayed itself to me in its full force, and which must, in due course, be recognized in practice. At

the meeting in 1907 of the British Association, Prof. H. E. Armstrong read a paper on "Enzymes, their Mode of Action and Function," in which, after observing that "the distinctive feature of the chemical changes going on in the bodies of organisms was the fact that they are under the *control* of the bodies called enzymes" (Report in *Nature*, Sept. 26, 1907), he went on to state, as "one of the outstanding conclusions" of the recent study of enzymes (or ferments), that "all chemical equations involving their action are to be written as reversible changes." This obscure but momentous question of the reversibility of ferments is still in its very beginnings. I call it momentous, since, life being a series of fermentations, it foreshadows amazing possibilities as to turning backward the finger of time for living creatures generally—possibilities so stupendous that I will refrain from expressing them more explicitly. But this question of the reversibility of all ferment action obviously concerns us as regards the ferment treatment of cancer; and it may yet be found that our highest hopes can be consistently realized only when we have elucidated and can control the conditions which determine the direction of the ferment action.

With these considerations before me, it would be the merest quackery to attempt to define the higher claims of the treatment without reserve or qualification. But it must surely suffice to place before the public and the profession the evidence which proves that, at any rate, results of the most merciful and invaluable kind have actually been obtained, and are now being obtained, in cases far beyond all hope from the knife or any other mode of treatment hitherto practiced. For such results many persons now alive are deeply indebted, and their number

can be indefinitely increased in this country if and when my solitary but soon to be reinforced voice is listened to; but meanwhile we are only at the rude beginnings, and the best is yet to be: "There are many events in the womb of Time which will be delivered."

I do not claim that the treatment is rapid. Assuming the relevance of the facts, we may note that Nature, dealing with trophoblast of only seven weeks' development, and without surgical operation, takes several months to dispose of it, and that degenerate remains of trophoblast can be observed in the normal placenta at full term. The present estimates of length of the treatment may some day be found adequate—when primary and untouched cases come under a perfected method: they are too brief, much too brief, when applied to the advanced and post-operative cases which for some time to come will furnish the majority of cases. In more cases than one the treatment has been stopped prematurely with disastrous results. The primary growth may appear to be dead, but it very likely has been accessible to local application as well as to application by the blood, and it does not follow that, because it is dead, secondary growths, unseen and perhaps unsuspected, are dead also.² I believe that the paragraph previously quoted in this chapter, from Dr. Cleaves, much more nearly represents the truth of this matter than estimates formerly made, and I warn the practitioner against making promises, or even finite estimates at all, as to the probable length of time during which treatment will be required. It may possibly be

²Also, a tumor apparently dead may not be dead to its very center, which is nourished only at second-hand, so to speak, by the lymph which exudes from the blood-vessels at the periphery. No malignant tumor produces blood-vessels of its own.

that the case is really analogous to that of the treatment of myxœdema by thyroid extract, though I do not think that this is actually so. It would only necessarily be so if the growth of cancer were due to defect of the pancreas, a supposition which is not warranted by the present evidence.

I make no prophecy as to the ultimate place which trypsin and amylopsin, as against other cancrotoxic ferments, will take in the treatment of cancer, nor as to the effect which their use will ultimately have upon the relations between cancer and surgery. Many things may be hoped and expected, but "*qui vivra verra.*" Meanwhile, I am content to claim for the treatment that it demands employment in every case of malignant disease without exception, whether other treatment be employed or not. Already it may be said that it is apparently no longer necessary for any one within reach of these ferments in an active state to suffer from cancer cachexia, from the fœtor, or from the pain of the disease. If I make no further claim at present, it is because there should be much more than sufficient to insure for the treatment as wide a trial as could any claims whatever.

There may be noted here a possible contributory explanation of the results of the ferment treatment in its various forms. It is well known that in many, indeed most, diseased conditions, the number of white cells or leucocytes in the blood is found to be increased. This leucocytosis, as it is called, was at first regarded as a pathological symptom; it is now conceived as a protective, conservative, or compensatory mechanism. Thus the cases of pneumonia—a disease usually marked by high leucocytosis, and ending in most cases by spontaneous recovery—in which leucocytosis does not occur are com-

monly the fatal cases. Some measure of leucocytosis is common in cancer, and, in all probability, this is one of those significant and invaluable facts hitherto practically ignored in the study of the disease, since the surgeon, for instance, cannot stitch a leucocyte, and it is, therefore, less than "Hecuba to him." Dr. Lovell Drage, whose phrase about the "stopping power of the old gang" in reference to new forms of treatment for cancer comes to mind, has lately shown (*Lancet*, Sept. 7, 1907) that favorable results, up to a point, may be obtained in the treatment of cancer by the use of drugs which are known to increase the number of leucocytes in the blood-stream. It occurs to me that the use of turpentine in uterine cancer—for which Chian turpentine was at one time regarded as curative, so useful is it—may be thus explained, since the group of drugs to which turpentine belongs (loosely called the volatile oils) are known to cause leucocytosis. Suggestive, also, is the observation of Prof. Farmer, that at the edge of a cancer the leucocytes seem sometimes to be merging into the cancer-cells. We may note this without accepting the surely wild suggestion that cancer may be due to this kind of unnatural union. I should rather be inclined to interpret it as evidence of the manner in which the leucocytes attempt to fight cancer. Everything we have known about leucocytes since the great work of Metchnikoff some decades ago, together with the fact of leucocytosis in cancer, lends probability to the supposition that the leucocytes fight the alien cells of the growth as they are known to fight alien microbic and protozoan cells, such as those of malaria and infectious diseases in general. In all cases whatsoever the weapons used by both sides are doubtless ferments; and I am perfectly willing to entertain the supposition that the leucocy-

tes produce a cancrotoxic ferment, and even that this may possibly explain Prof. Bier's results. I have no prejudice in favor of trypsin or any other ferment, need I repeat? Further, the work of Schmidt, who showed that cancer-cells, after eroding a blood-vessel and entering the blood-stream, are often occluded and destroyed there, not only directs attention again to the blood as a holder and carrier of cancrotoxic ferments, but specially directs us to the leucocytes. The invading cells are seen to be surrounded by a blood-clot, which pins them, so to speak, against the wall of the vessel. Now, all blood-clots are known to owe their origin to the stimulation of the leucocytes, which produce an antecedent of the so-called "fibrin-ferment"; this, in the presence of lime salts, inducing coagulation of the formerly fluid fibrinogen of the blood serum. It is possible that the leucocytes may not only begin the work observed by Schmidt, but may continue it.

In this connection the observations so minutely and extensively made by Dr. Cleaves are worthy of note. She found not merely an extraordinary increase in the numbers of leucocytes of a certain type, but also a marked and practically immediate increase of the leucocytes in general, under the pancreatic treatment. Surely there is abundant reasoning for crediting and investigating the supposition that this leucocytosis plays a part in the production of favorable results by the treatment. I would note also the hypothesis favored by Dr. Cleaves and Dr. Beard, that the specific effect of the amylopsin, or one of its effects, may be to stimulate the leucocytes and aid them in the work of removing the glycogen from the tumor, in which it has been produced by the proteid-splitting action of trypsin—this glycogen appearing in the leucocytes as the eosinophile granules. These obser-

vations are in need of confirmation, and may be commended for that purpose. But in any case it is evident, I think, that the question of the production and function of leucocytosis in cancer is one that demands the serious and systematic investigation which it has not yet received. What, for instance, is the leucocyte count in cases of spontaneous cure? Like the many other questions of great moment which may be asked regarding these cases, this is at present without an answer.

The thymus gland is supposed to be a source of leucocytes, and the spleen certainly is. Thymus preparations, according to one observer, are cancrotoxic in some degree. I should recommend the spleen for study as a possible source of a cancrotoxic ferment or ferments—which may be leucocytic or really derived from the pancreas, but the extraction of which from this gland would be of interest.

What are the fallacies to look for? Immeasurably the most important in the case of this disease is the fallacy dependent upon a false premise. If the disease is not cancer, violet-leaves, molasses, or any other irrelevant rubbish may seem to cure it. In the first case of cure recorded, that of a cancer of a vocal cord, no microscopic examination was made. It might have been an innocent tumor. I do not think any one could read the account of the case and think so, but still in itself it was not conclusive. But the reader is now aware that more or less successful results have been obtained in many cases where the nature of the disease was far beyond question, whether by the naked eye or the microscope—where, indeed, it had again and again recurred with every malignant character in evidence. The second fallacy—though this is

only to be mentioned for form's sake—is that dependent upon the fact that perhaps once in fifty or one hundred thousand times a true malignant tumor will spontaneously degenerate and disappear. This is almost the rarest occurrence known to pathology. In Mr. Handley's recent monograph, *Cancer of the Breast* (Murray, 1906, p. 156), is reported "the most convincing" of the cases of spontaneous cure that are on record. Doubtless there are other such cases, and at the Heidelberg Conference on Cancer, in September, 1906, there was a tendency to admit that the spontaneous cure of cancer is somewhat less rare than used to be supposed.

At this time of day it is no longer necessary to adduce arguments against the view that in every case where the pancreatic treatment has seemed to cause the retrogression of a cancer, the disease has really been undergoing spontaneous cure. The results have been repeatedly observed in various parts of the world in cases which, until the treatment was employed, were visibly active, and where the growth was increasing rapidly in size. This was the case with Dr. Beard's mice, though the argument has been absurdly raised by persons who apparently did not read the account of the experiments, that the tumors were undergoing atrophy in any case. This argument against the results of the pancreatic treatment could not possibly be alleged by any one who had watched properly treated cases for himself. This, however, is exactly what not one in a thousand of the critics have done.

In the first case I watched—it was under the care of Dr. Bonnefin of Leytonstone—in February and March, 1906, I found myself constantly doubting whether the evident disintegration of a uterine cancer under the treatment was not due to bacterial action—even though the

previous foetor of the case disappeared. This fallacy has long ago been excluded by experience, but Prof. Von Leyden and his workers have paid special attention to it, and shown that the results following the use of trypsin are due to a true ferment action, and not to accidentally synchronous bacterial disintegration of the growth. This possible source of fallacy does not exist in unexposed tumors.

Though an excessively minute percentage of cases of malignant disease undergo spontaneous cure—a fact which in itself shows that the remedy for cancer must be sought in the tissues and secretions of the body—the number is so small that only a surgeon here and there has ever seen such a case—much less a recurrent case, such as have furnished the majority of our patients hitherto. For practical purposes, then, the treatment of cancer is not subject to the capital fallacy which makes nine-tenths of all therapeutic claims at the present day ridiculous. When I was a student I worked in two adjacent wards, in one of which the proper answer to a question about chorea was that cases last in general for about six weeks, the symptoms then spontaneously disappearing; while in the other the answer desired was that, in general, arsenic cures chorea in about six weeks. The point for the judicious, if dishonest, student was to remember whether he was in (say) ward 28 or ward 29. In his "Address in Medicine" to the British Medical Association in 1907, Dr. Hale White, pleading for "accuracy of thought in medicine," pointed out other cases of the kind, such as exophthalmic goitre. In general, patients die of a disease or recover from it—the word cure, as applied to the doctor's interference, is entirely inapplicable. One might as well say that most cases of pneumonia are cured

in ten days or so, or that the doctor cures bronchitis in a fortnight; while it cures itself in two weeks, as the Irishman observed. This fallacy, and that of attributing the result to one agent or another according to taste, such as creasote administered to a consumptive who is also undergoing the open-air treatment, infest and vitiate to-day nearly the whole of medicinal therapeutics, which, in the average hands, is simply the licensed administration of poisons in something under lethal doses, as a rule.

In the treatment of cancer, and the estimation of the results, these fallacies can be excluded without difficulty. Almost invariably—so constantly that it would be difficult or impossible to find any observer who had seen two exceptions—the disease proceeds, though with varying pace, to a fatal termination. If in two consecutive cases it disappeared under hypnotic suggestion, the presumption would be practically overwhelming that this agent had effected the cure. The argument of spontaneous cure was to be considered when the first case was recorded: the second sufficed to dispose of it substantially, and it has long been out of the question. The other source of fallacy is relevant in cases where the Röntgen rays have been employed, and, of course, in post-operative cases where the surgeon has apparently removed everything. Such cases must be individually analyzed. In the absence of any other agents which mechanically or otherwise are capable of curing cancer, favorable results must necessarily be attributed to the pancreatic ferments themselves. Many such results have been quoted already.

If, however, the phrase is for any reason preferred, let it be stated that, when the pancreatic treatment is properly employed, cases of cancer commonly show a tendency to undergo spontaneous cure; or let it be reported that,

in spite of the pancreatic treatment, the patient recovered or was benefited—as might be reported after so many therapeutic adventures. If the critics will take the thing from us, we will take any words they please from them.

I claim, therefore, that the capacity of the pancreatic treatment to cure certain cases of cancer has been absolutely demonstrated, though it should never cure another. Nature is consistent, however, and the application of her methods will do in the future what it has done in the past. Trypsin is a specific remedy—whatever others there be—for cancer according to the embryologist in his study; it is the specific remedy for cancer according to the chemist with his test-tubes; and it is the specific remedy for cancer according to the clinician at the bedside.

A grave and inevitable responsibility now rests, therefore, upon all editors, surgeons, official researchers, patients' friends and patients themselves, who by word or writing or act oppose the employment of the new treatment at any time in any case of malignant disease. An appalling indictment may be framed upon those, mostly an anonymous and ignorant assemblage, who, during the past two years or so, have fought this method, whether fairly or unfairly, whether with the rare argument or the familiar lie. Some forty-five thousand persons have died of malignant disease in Great Britain alone since I began my campaign on behalf of a method which, from the first, was reasonable, supported experimentally, free from risk, and without an effective rival in the world for the vast majority of cases, surgery notwithstanding. The question is one of life or death, of ease or agony, for very nearly all the sixty to one hundred thousand persons now suffering from cancer in Great Britain alone, and many hundreds of thousands elsewhere. I submit that, despite

the legitimate or inherent and the illegitimate difficulties of the past two years, the treatment has now established a claim to trial, if not indeed to universal applause, which cannot be resisted. When this book was begun, more than a year ago, I was still in some doubt whether it would ever see the light, whether my labor was not worse than wasted. On the other hand, there was a reasonable chance that if I did as much work as possible, even while much doubt remained—doubt which perhaps had no more basis than the psychological fact which leads us to say that a thing is “too good to be true”—at any rate, if and when the evidence proved convincing, no priceless time need be lost before publication: here time was not money but life, many lives: and ease for agony. Now that the evidence has been published and the claims of the new treatment set forth to the best of my ability, the grave responsibility of delay, which has so long haunted me, is transferred to the shoulders of the public at large; they alone will be to blame if the new hope offered them—offered to those who have no other hope in the world—is renounced. My experience has been that, for one doctor who has written to me, dozens of patients or their friends have written; and it is evident that the patient, and those who love the patient, must on the whole be more eager for a remedy than even the most humane or ambitious doctor. I have therefore given this book as popular and arresting a title as I could think of; I have not gone to the ordinary publishers of medical books; and I have attempted the almost impossible task of writing a book which will be intelligible to the layman and useful to the practitioner and the scientific student. To these last I express my regret for explaining what they know, and for the clumsiness which is almost inseparable

from the avoidance of our convenient technical phraseology; but it was necessary that the public should read and act without delay, and I have chosen the means best suited, as I believe, for that end. This book is written for the man or the woman who has cancer; only incidentally as a study in sociology, or as an account of certain scientific observations, or as a tribute to one whom I regard as a pioneer of genius. It is therefore to be judged, not by its title nor its style, nor its candor when dealing with what the author rightly or wrongly believes to be dangerous obstructions to truth, but by the validity or invalidity of the claims which have been made for the treatment in this chapter, and, if those claims be found valid, by its fitness for the urgent purpose of multiplying to the uttermost and at the earliest, the number of those, otherwise substantially hopeless, in whom its claims may be realized in whole or in part. Let the reader imagine that he himself has an inoperable cancer—if he is as old as thirty-five, the chances are one in twelve that this fate is in store for him, and for a woman they are as high as one in only eight. Let him then condemn me as “premature” if he can. The word has been thrown at me often enough, and it is the least offensive of many that have come my way, *but it has not yet come from a patient*. And as “one wise man’s verdict outweighs all the fools,” so one patient’s verdict on the claims of this treatment outweighs all the verdicts of all those who, in no need of help themselves, have denied the existence of that which they could not or would not see, and the reasonableness of that which they could not, or would not, understand.

If I have been censured once I have been censured twenty times for “exciting false hopes” by my crusade

on behalf of the new treatment, or rather, on behalf of the cancer-patient. I have been accused of criminal and brutal cruelty, and so forth, by the leading medical journals in England, and by some of the lay papers in America. Here I will expose this argument for the grossly dishonest and puerile thing it is. I might argue that even hope may be worth something in itself, or that the question of the falsity of the hopes I aroused—hopes in many cases justified—was begged by these writers; but these arguments need not detain us. We need only note, in the first place, that certainly in the majority of cases of operation for cancer—and the number of these is gigantic—the surgeon arouses hopes of cure. At least he will say that he will do his best, though he can promise nothing: and on these terms he is permitted to operate. What proportion of all the surgeons who daily arouse these hopes in their patients have ever justified them in a single instance? I am content merely to ask the question, and I do not by any means suggest that the suggestion of a chance of cure is improper, though the chance be only infinitesimal.

But, secondly, in answer to the *British Medical Journal*, the Bradshaw Lecturer of 1906, and all the others who have censured me on this ground. Is it not the rule, rightly insisted upon and almost invariably practiced, that the word cancer shall not be mentioned before a patient? Does not every doctor regularly and rightly keep the patient unaware of the nature of the disease as long as possible, informing only a responsible relative? Every one knows that it is the duty of the doctor, a duty to which every medical student is trained, a duty which leads to the use of all sorts of euphemisms for the word cancer, to excite or encourage in his cancer-patients hopes

which he knows to be absolutely false. This being the recognized duty of the profession, its spokesmen have the rare effrontery to blame me for exciting hopes which I believe to be well grounded. That they have in many cases been proved to be well grounded adds nothing at all—because nothing can be added—to the weight of my reply. It is the duty and practice of the profession, not only in cancer, but always, except for special reasons—as, say, the need of making a will—to “keep up the patient’s spirits,” remind him that while there is life there is hope, conceal the name of a dreaded disease and its nature as long as possible. This is deliberate lying, of course, but, in common with all the world, I defend and approve it. Now if all mankind is justified, on the grounds of common humanity, in exciting hopes known to be false, I will permit myself the license of exciting hopes I believe to be true. Of all the impudent and disingenuous things that have been said about trypsin and its advocates, I think this is perhaps the foremost, though I would not care to be too sure.

I have claimed for this treatment that it should be employed in all cases of malignant disease. In no case that I have submitted to Dr. Beard, on application from readers of my articles, has he suggested that the case was unsuitable, and repeatedly it has been employed in cases where success was absolutely beyond all possibility. (Several of the Middlesex Hospital cases were quite obviously of this kind.) But even if there was no credible chance of cure, there was the incredible chance, and I honestly believe that the idea of picking his cases for treatment, as is constantly done by physicians and surgeons all the world over when they are trying to prove the value of a method, has never entered Dr. Beard’s

mind. I quote from Dr. Macfie's admirable little book, *The Romance of Medicine*, a paragraph concerning another scientific worker, like Dr. Beard, "not even a medical man," but a supreme benefactor of mankind and the greatest master of medicine of all time hitherto:

"And Pasteur was not only kind, he was also noble and magnanimous. When his treatment for hydrophobia was still *sub judice*, when his reputation depended on its success, a little child was brought to him bitten, thirty-seven days before, by a rabid dog. It was almost certainly too late to save the child, and Pasteur's assistants pointed out to him that if the child died the death would be laid to his account and would discredit his discovery. They begged him, therefore, to make no attempt to save the child's life. 'No,' said he, 'if the child have one chance in ten thousand of recovery I ought to try everything.' And he gave the child the chance, and bore without flinching the opprobrium which her death brought to him."

That "the patient must have every chance" is the first axiom of medicine; and I claim for the pancreatic treatment that the patient who dies of cancer without any attempt to employ it, has not had every chance. I claim further that the cancer-patient has practically no other chance, and that, unless this primary axiom of the healing art be repudiated, neglect to employ the treatment will henceforth be—as it has been since the time when public attention was first drawn to the treatment—wholly without excuse or defence. The practitioner who fails to obtain beneficial results runs no risk of personal discredit, at present at any rate; the only persons discredited will be Dr. Beard and myself; but the practitioner who will attend to details, as the surgeon does in his work, will assuredly serve, and may save, his patient.

CHAPTER XVIII

SOME WARNINGS

HAVING put my hand to the plough in the matter of informing the public, to the best of my knowledge, regarding the progress of the war with cancer, and having myself suffered many hard blows meanwhile, I here devote myself to a matter in which I shall certainly be approved by all honest persons, whatever their attitude towards the pancreatic treatment of the disease. I believe I foresee certain all but inevitable developments of no desirable kind, against which I wish to warn the public. It would be a poor service to give hints for malpractice to the ill-inclined, but, unfortunately, it is impossible to doubt that the hints are unnecessary to his activity. The best course, then, is to point out the opportunities of which he will be certain to avail himself; so that the public, forewarned, may be forearmed. The most valuable prophecies of evil are not those of Cassandra, which always came true, but those which effect their own falsification, and it is such prophecies that I desire to make.

The work of Dr. Beard, the recent work of Prof. Von Leyden, with a supposed "liver-ferment," and of Prof. Bier with a "blood-ferment" of uncertain origin and nature, each of these having a proven remedial action upon cancer, offers, or will soon offer, rare and golden opportunities to the tradesmen—or rather, the dishonest and wholly mercenary tradesmen—who unfortunately cannot be excluded by any known means, universal publicity in all cases alone excepted, from the noble pro-

fession of medicine. It is a chance for the qualified—often highly-qualified—quack who is the curse of the profession. I think it quite certain that—failing my efforts to prevent it—the next apparent development in the treatment of cancer will be the introduction and exploitation of a new “cancer-serum.” The wonderful anti-diphtheritic serum has led the public and the profession to look favorably upon the word.

We often talk about the *vis medicatrix Naturæ*. Now, the work of Dr. Beard, and all who have subsequently labored in a substantial way at the problems of cancer, shows positively that the body itself, and not any vegetable or mineral or knife, can and does provide a specific remedy for cancer—this surely being the evident explanation at last of the spontaneous cures which, though excessively rare, do occasionally occur. Thus it is true that a “serum” derived from the liver, or the blood, or the thymus, or some other organ, may *conceivably* be prepared, which does not consist of the pancreatic ferments, masked under another name; and such a “serum” may prove more effective than trypsin and amylopsin—though this I may personally believe to be improbable. Now I elsewhere warn the reader against myself, on general historical principles, as a judge of anything that threatens to supersede the pancreatic ferments, but the warning is unnecessary here, for the public and the profession alike have a simple and infallible and costless means of judging for themselves. It will be attempted, unless, perhaps, this prophecy averts it, to produce a serum which, though the phrase will not be used by its exploiters, will in fact be *of secret composition*, asserted to be capable of manufacture only under the direction of one man—perhaps a German professor, perhaps a Parisian surgeon,

perhaps some one else. Some "institute" or other may ostensibly be the source of this wonderful preparation. We shall be told plausible tales as to its source in some gland or other, not formerly mentioned in this connection, such as the spleen, or any other the function of which is obscure; but the mode of preparation will not be confided to us. We shall learn merely that it is exceedingly difficult and costly to prepare, the processes being of infinite delicacy and requiring a great length of time; and that, since the gland in question is a small one, and the product highly concentrated, only minute quantities of the serum can be obtained until the resources of the "institute" are extended. The dose, however, will be somewhat large. Hence the expense will be enormous; but civilization has many millionaires, and many of these have, or soon will have, cancer.

This new serum will have an incalculable advantage over all cancer-cures, except one, that have hitherto appeared; it will be more or less effective. If well prepared it will certainly relieve pain, remove foetor, and abolish discharge where these exist. For such purposes it will require free local application, and I have already commented upon the grave expense of its incommunicable preparation. But it will do more or less what it professes to do: certain cases of well-authenticated cancer it may very possibly cure: all without exception it will probably benefit—being employed with great skill—in such an unmistakable fashion, and so quickly, that every one will have to recognize the fact—and the "resources of the institute" will be increased. However, there will always be only a tiny quantity just available for use—though never none at all—and this may have to be bid for by rival purses, probably American.

This is not an imaginary picture; my imagination, I hope, is not morbid enough or uncharitable enough for that. These things have happened before, and they will happen again, unless we can help it. I earnestly warn the public and the profession to beware of any such "serum" when it appears; and the warning is all the more and not the less necessary because, for the first time in history, it will doubtless be of some real value, greater or less. If trypsin and amylopsin can be superseded in the treatment of cancer—which, though I do not expect it, I certainly hope, for they lack ideal rapidity of action, as an instance—let the new discoverer give his knowledge for nothing, but everything worth having, to the whole world, as Dr. Beard has done from the first, like his peers of yore, Pasteur and Lister and Jenner and Simpson. If he be a medical practitioner he will not lose in the long run, even monetarily; and if, like Dr. Beard, he be not, at least he may gain gratitude, without having to face the abuse that has been Dr. Beard's portion and mine.

But if trypsin cannot—or cannot yet—be superseded by some other ferment (for a ferment it assuredly must be) still more powerful, not less safe, and more speedy, there is nothing but knowledge and judgment on the part of those whom I now attempt to forewarn, to prevent any one—and especially the highly qualified and famous variety of quack—from preparing a "serum," the essential part of which will be the pancreatic ferments, keeping its composition and mode of preparation secret, and following the unworthy examples of old and recent times.

The public is possessed of, or can obtain at any time, all the information that exists regarding the pancreatic

ferments. For that matter, any one may purchase, at a *fair* price, the splendid recent preparations of, for instance, the great American firm of pioneers in this path and may make a "serum" of his own without difficulty. The sole disadvantage to be set against the overwhelming advantages—money apart—of having no secret and telling all you know, is that thieves and liars exist who can and may use for their own nefarious purposes the knowledge supplied for the public good.

Doubtless the proteolytic activity of the "serum" could be readily ascertained, and doubtless in time its true nature would appear, but the men who have more money than judgment would be swindled meanwhile, and the thief would prosper exceedingly. All the conditions—such as the obscure nature of ferments, and the difficulty or impossibility of their absolute identification—make this fraud peculiarly easy: *but the test of it shall be its secrecy*, and no chemical test will be necessary if that one is conclusive. This test will exclude no real advance upon trypsin, if such be made. Meanwhile we may remind ourselves that, to current physiological science, trypsin is by far the most powerful of all known proteolytic or proteid-digesting ferments, and amylopsin similarly by far the most powerful of all known ferments of its class. It is quite possible that this warning may frighten off the thieves, and I will take my chance of being told that it was unnecessary, as I well know it is not. It can hurt no honest man.

So much by way of a warning to the wealthy, for whose especial benefit so many serums and unique methods of treatment exist—the marvelous operation that only one surgeon can perform being another variety of the same trick. We turn now from the wealthy patient and the

qualified quack, to the poor patient and the unqualified quack, and to the many who "do not believe in doctors," but will swallow anything in the way of lotions or lies from the man who professes to know more than doctors do. These two classes of people, each of whom we have always with us, suffer in their hundreds of thousands from cancer, and have long been the prey of the ordinary humble cancer-quack of all varieties. This cancer-quack is on his last legs, and very soon the final specimen of him will go to his unhonored grave, for the same reason as that which explains why there are no malaria-quacks. A malaria-quack could not stand up against quinine: it is only the disease for which no cure exists that the quacks profess to cure. But for a little while to come the cancer-quack, and the man who treats the people who do not believe in doctors, will have a rare harvest—unless the public will learn sense in time. The pretender need run no risks. He need not make any injections of the ferments, for mere local application to accessible cases—as most cases are or too soon become—will accomplish more than any means hitherto known have accomplished. This alone will usually abolish all discharge and all fœtor, and relieve pain—practically always if the man be competent. These results will be sufficient to substantiate his claim in the eyes of his patients, *for a time*, and he, too, will flourish exceedingly.

If he really does good, why should I seek to prevent him? Because I know that, except in the rarest and most superficial cases—if then—he will never cure his patient (assuming the disease to be really cancer), and because I know that infinitely more than he will accomplish may be accomplished by the injections *which he dare not make*. Formerly his pretensions were soon ex-

posed, and he was dismissed for the liar he was: now he may markedly benefit the patient, in *non-essentials*, for months at a time, meanwhile preventing the patient from undergoing the only adequate form of treatment. On the whole, he will be thus a far more pernicious person than before, even though he will be able to do *some good* now and could do none formerly. Quite apart from anything more, trypsin has absolutely substantiated its claim, in every case of exposed cancer, to control discharge and fœtor by its rapid and complete digestion of the dead and dying surface of a cancer, and this it does without the slightest pain—very much on the contrary—and without the slightest risk. In my judgment it is now criminal negligence, and should be regarded as professional malpractice, not to employ it for this purpose alone, even though the doctor absolutely denies that it can do anything whatever to living cancer cells. But see the power of the charlatan—a power of which, I hope, the methods of publicity which have proved so essential, and have been so much reprobated, will deprive him. The control of fœtor and discharge immensely improve the color, the appetite, and the general health of the patient—even though the tumor be growing as rapidly and actively as ever, or more so. I have no fear in making this admission. Thus the charlatan can give by the mouth any nostrum of his own, or the “healer” by sacred phrases or incantations can proceed with his methods, and they will get the credit of the general improvement. Voltaire remarked that “incantations and arsenic will kill any number of sheep”: and incantations and a little trypsin locally will do wonders in any exposed cancer: but the patient is being killed by inches all the same, though I admit that the control of the fœtor and discharge may, nay,

almost always must, of themselves prolong life. If the proper treatment could do no more than merely local treatment will do, the charlatan and the "healer" might be left alone: it might be a duty to recommend trypsin to them, since so it might benefit persons who "don't believe in doctors": but trypsin can do far more, and so it is a duty to interfere with the charlatan and the healer, who dare not apply the complete treatment, and, having never heard of Lister, would doubtless cause lamentable abscesses if they did.

Yet another prophetic warning: and this for the average sensible middle-class man, whose purse is too small to tempt the qualified vender of secret serums, and who has too much sense to deal with the cancer-quack, or those who profess, honestly or dishonestly, to cure cancer by Christian Science or the like—cancer, like decayed teeth, being one of the few mountains which even faith will not move. The cancer patient belonging to this class, safe from the foregoing risks, has risks of his own to run. He is familiar with the fact that surgeons differ widely in skill, and that their fees differ accordingly, as they should on all sound principles of economics or justice. He knows that no monetary sacrifice of which he is capable is too great if it means the difference between the surgeon who *may*, once in many times, effect an absolute and final cure, and the surgeon who always leaves part of the disease behind. Now it must be made clear that the case of the pancreatic treatment is quite different. I will not say for a moment that it is on all fours with the treatment of malaria by quinine; for it is a matter needing cleanliness in the surgical sense, assiduity, patience, conscientiousness and other qualities which are not too common. But though it makes requirements

which are not universally to be obtained, they are requirements which can be often met. They are not requirements which leave or should leave any room in the future for any such person as a "cancer-specialist," and the fact is worthy of insistence. My experience of the past two years, or little less, abundantly shows that prominent and famous specialists—outside Germany—may fail, from sheer carelessness, or the lack of faith which leads them to blame *the* method instead of *their* method; while the ordinary practitioner, devoting himself to the case, and not above consulting non-practitioners like Dr. Beard or myself, will succeed. There is no room, then, I repeat, and I believe there never will be room, for the "cancer-specialist," in the ordinary sense of the word, but only for the cancer-specialist who is a specialist in all diseases simply because he has the special qualities which make him a good practitioner. Such a man is entitled to his success in any field, and he earns immeasurably larger fees than he, or even the specialist so-called, ever receives: but it is not primarily fees that he is after, and therefore he will not pitch them too high. Therefore, I say to the ordinary sensible middle-class man, beware of the practitioner who demands exceptional fees, and of his claim that he is a specialist in the treatment of cancer. No conceivable device will keep this kind of man out of the profession, in which the colossal ignorance of the public affords him countless opportunities; but his deeds will betray the mark of the beast to those who look for it, and the outside of the sick-room door is his appointed place in this world, whatever be his prospects hereafter.

Beware, also, of the man who promises too much, or rather too little, in the matter of time. We do not at all

know the nature of the conditions which permit the growth of cancer: that is a point, and a most important one, elucidated in no degree, so far, by Dr. Beard or his great German followers: though I believe it will shortly be explained. Meanwhile it is possible that, as Dr. Cleaves hinted in her admirable paper in the *New York Medical Record* (June 1, 1907), in some cases, if not in all, the use of trypsin may have to be continued, perhaps only at intervals, throughout life; just as the use of the essential secretion of the thyroid gland has to be continued throughout life in cases of myxœdema and cretinism. The man who promises that the treatment will only require a few weeks or months, and that thereafter the patient will be cured and remain cured, without fear of any recurrence, and without any further need of trypsin, may happen to be right, but he is an ignorant man of the worst type, one ignorant even of his own ignorance. Let such be shunned.

Normal trophoblast begins to degenerate about the seventh week of ante-natal life, but its remains can be detected at birth. Dr. Beard insists that the process of the digestion of normal trophoblast is very slow, lasting for many months; and so, especially in cases operated upon and thus stimulated by the surgeon, may we expect the digestion of "irresponsible trophoblast," or cancer, to be slow, even under the best treatment. Beware, then, of the man who promises too much in this respect.

Though the treatment is necessarily prolonged, except in the early and favorable cases, not one of which has yet come under treatment in any part of the world, so far as I know, its cost, per week or month, has no occasion whatever to be appreciably higher than medical treatment in general. The doctor's visit need be of only the usual

average length, and the pancreatic preparations are much less costly than a host of commonly used drugs, if these be of good quality.

I issue all these warnings because, from the very first, I have been writing and working in the interests of the public at large, and because I have no desire, on the other hand, to benefit any individual practitioner or group of practitioners or chemists. I write, as I have written—not primarily for the medical profession, nor for the surgeons, as is evident enough—but for *the man and the woman* who have cancer:—at any given time sixty thousand in Great Britain alone, according to one estimate, and a hundred thousand, according to another, and a more probable one. I believe this chapter will serve them, and those who love them, and I will content myself with *their* verdict on it. The critic who has not cancer I am entitled to ask the grounds of his interference. Is he a surgeon who lives largely by operating on the disease, for instance, or what is he, and what is his business with it and knowledge of it? Let us, as a novelty, have his name. One man in twelve, and one woman in eight, over the age of thirty-five, die of this disease. Let the critics wait a little till they, in their proportion, have cancer, and their business with my writings is indisputable. When their turn comes, as it inevitably will come, to many who have criticized and condemned, while utterly failing to provide that real criticism of which every new discovery is in particular need, and which this has never had from outside, I hope with all my heart that they will renounce all consistency and give the new remedies the full and early trial from which they have dissuaded so many of their fellow-beings who were without other hope or help in all the world.

CHAPTER XIX

AMYLOPSIN AND ECLAMPSIA

THE present chapter, it must be recognized at once, is in the condition of Dr. Beard's theory of the nature of cancer when it was first announced in 1902. That is to say, it is wholly theoretical or speculative, and is, at present, without any kind of experimental basis. There is known to the obstetrician a terrible disease which is called eclampsia. There is nothing which he fears so much, since there is nothing for which he can do less. It is said to occur in one case of pregnancy in about three hundred and fifty, and most commonly in first pregnancies, as also in cases of twins. The symptoms are those of poisoning of the nervous centers. Those first observed "consist in complete or partial, temporary or permanent, loss of vision, flashes of light before the eyes, vertigo, headache, drowsiness, mental depression, nausea and constipation." Albumin is found in the urine. These symptoms may lead up to most aggravated and dangerous convulsions. The treatment is extremely unsatisfactory, but if the patient survives the emptying of the womb she will almost certainly recover.

There are many and various theories of the nature of this disease. There is no need here to discuss those which are demonstrably untrue. Undoubtedly that for which most support exists is the theory of Stumpf, that the fits are due to the circulation in the blood of some poison

produced by an abnormal decomposition in either mother or child. He believes that under abnormal processes of decomposition a substance free from nitrogen, toxic in its action, perhaps acetone, or a body resembling it, which reacts to the same test, may be formed. This theory has recently been supported by Fehling.¹ According to him, it may be that the metabolism of the foetus and the transference of the foetal products into the maternal circulation are of more importance than has hitherto been supposed. The nephritis of pregnancy is, he thinks, most probably not the cause of eclampsia, but the first sign of intoxication, of which the actual fits, if they supervene, may be the second. The predisposition to eclampsia in the case of multiple pregnancy, and the great improvement which follows emptying the uterus, are strongly in favor of the supposition that the poison is produced in the child. Another observer believes that the disease is due to intoxication by poisonous ferments which arise in the placenta, a supposition which immediately suggests the ferments of trophoblast or cancer.

Now in the early stages of the treatment of cancer by trypsin, before the importance of amylopsin was recognized by Dr. Beard, symptoms were frequently observed which had a very marked resemblance to the earlier symptoms of eclampsia, and among these was the occurrence of albumin in the urine. This observation seemed to Dr. Beard to afford some further support to a theory of the nature of eclampsia which, it is not impossible, may yet be verified. The theory² is that in the case of eclampsia, and in the case of the treatment of cancer by trypsin

¹*Encyclopædia Medica*, vol. III, p. 174.

²See the "Interlude of Cancer," by Dr. Beard, *Medical Record*, Feb. 2, 1907.

alone, the symptoms are due to one and the same cause—the absorption into the blood of products of dead and degenerating trophoblast. Dr. Beard believes, as we have seen, that the normal trophoblast is killed at the critical period—the seventh week in man—when the pancreas first begins to form trypsin. But, as we may remember, the pancreas of a human foetus and of a child until the age of one year produces no amylopsin—this being the reason why a baby cannot digest starch. Dr. Beard believes, then, that it is the amylopsin produced by the pancreas of the mother which completes the digestion of the foetal trophoblast. This is a long process, for remains of dead trophoblast can be found in the placenta after birth. Says Dr. Beard, “In normal gestation, if anything went wrong with the maternal pancreas gland, and if the maternal supply of amylopsin became diminished, or ceased, then serious symptoms were bound to follow.”³ To my question why, if this theory be correct, the symptoms of eclampsia usually appear late in pregnancy, whereas the trophoblast is killed as early as the seventh week, Dr. Beard replied that, though the trophoblast is killed at the critical period, there is then only little trypsin being formed; “later, as the foetus grows and grows, it produces more trypsin, and, therefore, more products of its activity.”

Like all other theories, this must be put to the test of experiment, and the experiment must obviously consist in the injection of active amylopsin in cases of eclampsia. So far as I know, at the time of writing, amylopsin has not been used by any one in any such case. The disease, however, is terribly common, and there exists no specific

³The pancreas is found to be seriously damaged in these cases, though the damage is not peculiar to this organ.

remedy for it. Injection of amylopsin is without the smallest danger, and causes very little local disturbance, or none at all. Physicians may, therefore, be counselled to make observations on this point, for it is not impossible that these may show them to have been armed by Dr. Beard with the true specific remedy for this disease. It is, at any rate, the general experience of the physicians who have employed amylopsin in the treatment of cancer, that it does control the constitutional symptoms which may be set up by the use of trypsin alone in that disease, and the resemblance of these symptoms to those of eclampsia cannot be ignored, especially if the existence of degenerating trophoblast in the pregnant uterus be remembered.

PART III—SOCIOLOGICAL

CHAPTER XX

THE POWERS THAT BE

“They take to criticising me a little more in the Reviews, and God send I be not proud of their abuse, for there is no hiding the fact that it is of the proper old drivelling virulence with which God’s elect have in all ages been regaled.”—From a letter of ROBERT BROWNING.

“Yet when the new light which we beg for shines in upon us, there be who envy and oppose, if it come not first in at their casements.”—MILTON’S *Areopagitica*.

No new truths required.—Proposed motto for any institution.

THE history of all progress—whether physical, intellectual, moral, social or artistic—is a history of revolt against *the thing that is*. Involved in the very idea of advance is the supersession of what is already established—whether a creed, or a practice, or an authority, or an æsthetic canon. The new—which may, of course, be worse or better than the old—is known in biology as variation, and variations are the raw material of all organic evolution. Those that endow the creatures who display them with fitness for life are selected by Natural Selection, while those that do not are rejected. Thus progress has been effected.

In the supra-sensible world the same law holds. All human progress has been effected by individuals, by individuality, and by the psychical products of individuals:

never by committees or crowds. Every truth began as a heresy. Institutions imitate, individuals initiate; institutions copy, individuals create. But just as in the realm of organic evolution, so in the realm of super-organic evolution, the good is the enemy of the better, the half-truth of the whole truth. The powers that be set their face indifferently against everything that is new, whether it be good or bad, an improvement or a deterioration. This is necessarily so, and involves no moral condemnation of established things. Were it not for this principle of conservatism or orthodoxy, which in the organic world is called heredity, there could be no surety for the persistence of the good; we should have no hold at all upon what our fathers have won for us.

But, on the other hand, this conservative principle has ever and inevitably involved the temporary postponement and precariousness of the new that is better—the worthy variation. It sometimes remains a problem for the biologists to understand how it was that the new thing—such as, say, wings, or a central nervous system—was able to hold its place while it was in an immature state. It would survive in virtue of its survival value when it was sufficiently well developed to be effective; but it must have had a hard time in its ineffective youth, when its presence embarrassed rather than aided its possessor.

And it is profoundly true of new truths or new ways of thinking, that their case is hard in the early days. The founder of ethical science was compelled to drink poison on the ground that he was a corrupter of youth. The Supreme Exemplar of the ages was crucified as a blasphemer, and the Florentine monk who sought to reform the established authority which called itself by His name was burnt at the stake. Ever the way of trans-

gressors—the word being used in its etymological sense—is hard. They cross the path of the many and the powerful, and must pay the price for so doing.

Those human activities which are concerned with the quest of truth, and which we call philosophic and scientific, are no exception to the rule. The powers that be seek to maintain themselves in being; it is not in the nature of things that they should do otherwise. The truth, or nearer approximation to the truth, that began as a heresy, ends as a superstition. Socrates was poisoned, but the doctrines of his pupil's pupil came to dominate Europe. A professorial colleague of Galileo declined to look through his newly invented *occhiale*, or telescope, at the moons of Jupiter, because they were not mentioned by Aristotle, and their existence was, therefore, unthinkable. The ceaseless persecution to which the great astronomer and physicist was subjected had its origin in the resentment which he excited in the followers of Aristotle—the powers that were—by his experiment of dropping balls of various weights from the leaning tower of Pisa, thereby demonstrating the falsity of an assertion made by their master. In the same land and age, Giordano Bruno, the first philosopher to form a true conception of the nature of the cosmos, was burnt for opinions which are now familiar truths; and, in our own time, when the author of the doctrine of universal evolution died, he was truly described in the *Fortnightly Review* as “him whom all the world outside the walls of our universities mourns and honors to-day.”

Conspicuous and exceedingly important among the modern powers that be is the medical profession, and it is worthy of note that, such is human nature, established authority is true to itself in the realm of science as in

the realm of theology. It is part of the ideal creed of science and her followers that there is no authority but truth; and her history, as she rightly insists, is the history of the struggle between superstition and theological authority, with all their tremendous power, and the new truths which, in the beginning, have had for their support but the voice of one man—and the unconquerable power which is part of the appanage of all truth. Lately, however, scientific doctrines, like theological doctrines, have become established, have been elevated to the rank of formal creeds and accredited dogmas; and the principle of the repudiation of authority, which was so easy of acceptance when the authority was extra-scientific, has become complicated by the emergence of scientific authority. Hence, since the days when scientific opinions, instead of being merely the teaching of this man or that, first became *established*, scientific intolerance has vied even with theological intolerance, and with infinitely less excuse, as consideration of the respective assumptions of science and theology immediately shows. Here we may confine ourselves to medical and surgical science, and to those recent days in which it has achieved such great triumphs.

Anæsthesia and antiseptics, with all that this last implies, represent the two great achievements of the medical sciences in the last century—or, indeed, in any century. Let us briefly consider their history.

In the domain of surgery the established powers were, of course, the surgeons. It was not from a surgeon that the advance came; and this principle, that the advance comes not from the powers that be, but from without, is illustrated most abundantly before and after the discovery of anæsthesia. A conspicuous protagonist of the em-

ployment of anæsthetics in surgical operations—though not actually the first man to make such employment—was Sir James Simpson, of Edinburgh. He was not a surgeon, but an obstetrician. Even in his own department he was bitterly, persistently, and all but successfully opposed by the powers that were, while they were keenly supported by the clergy, who denounced as blasphemous and impious the attempt to abrogate the curse pronounced upon Eve—"In sorrow shalt thou bring forth." These persons, protesting against the mitigation of pains which they could never be called upon to endure, were only silenced when Simpson, obeying the injunction to "answer a fool according to his folly," observed that the Lord God had employed anæsthesia in the first surgical operation on record, since He caused a "deep sleep" to fall upon Adam, before the excision of the rib which was converted into Eve. As for the surgeons, their hatred of the interloper and his success can be realized only by those who lived in Edinburgh in those days, or have heard of it from those who did so. In a word, the introduction of this unspeakable boon to all mankind, patients and surgeons alike, was opposed, tooth and nail, by the surgical profession of the day.

But let us turn to the history, more remarkable still, of the actual pioneer in this matter, Dr. W. T. G. Morton, of Boston. He it was who, in 1846, after plucky experiments upon himself—not to mention his favorite dog—gave the first public demonstration of surgical anæsthesia. He was then only a medical student. He is now commemorated, over his grave near Boston, as the "inventor and discoverer of anæsthetic inhalation; before whom, in all time, surgery was agony, by whom pain in surgery was averted and annulled, since whom science

has control of pain." But what were the facts of his lifetime?

He was beset by after claimants, one of whom was proved to have denounced the discovery as a dangerous practice for months after Morton's epoch-making demonstration. "No one unfamiliar with the story of the attempts to rob him of his just merits through twenty-one years of bitter attack, including ten years of vain struggle with the government for even a most modest recompense, can realize at this day the weight of the powers of adversity which beset his course. . . . Having spent a very considerable fortune to introduce his discovery and defend himself from attack, he was reduced to poverty. It was not many years until life itself was quietly crushed out beneath the load. The discovery of surgical anæsthesia, while a boon to the world, was a tragedy to its author and to his family: . . . his life was the one single life unblessed by what was to others blessing." As Dr. Weir Mitchell has said,

"We took the gift so humbly, simply given,
And coldly selfish—left our debt to Heaven."

Though this magnificent gift to that generation, to ours, and to all that are to be, could not be refused, at least the powers that were could wreak their vengeance on the giver, and he died, a broken-hearted man, at the age of forty-eight.

Now it is a noteworthy and significant fact that Prof. W. J. Morton, whose splendid pioneer work in America, begun not three months after the publication of Dr. Beard's mouse experiments, has been of inestimable service in furthering the treatment of cancer by ferments, is

the son of the great pioneer of surgical anæsthesia. This is, indeed, as it should be, and the name of Morton may go down doubly honored to ages yet unborn.

The next case was that of Pasteur and Lister. The French chemist is, of course, incomparably the greatest physician of all time, if language is to be rightfully employed; but he was not a member of the medical profession. Properly, he was a chemist, and while his great chemical teachers encouraged his labors in that field they frowned upon his excursions into biology—excursions which led him yet so much further afield. One English surgeon, now Lord Lister, had the insight and the courage to realize what Pasteur's work signified for his, and, as in the case of Simpson, the magnificent and immeasurably beneficent reform which he inaugurated was virulently opposed by his colleagues—the powers that were. We need not blame them, nor ascribe to them any peculiar villainy or hatred of the light. They were merely doing what the established thing always has done in all ages, and always will do until human nature has become angelic. When I was a student in Edinburgh there still survived a surgeon, a former colleague of Lister in the infirmary of that city, who had opposed the great reform, and though he had long accepted the heterodoxy (when it had become orthodox) we still knew him as “dirty —,” and handed on the graceful epithet to the new generation. But as in the case of Simpson, and as in all cases, if we but follow them to the end, the truth and one are a majority, and the successors of the men who rejected Lister find in him their chief pride. “The stone which the builders rejected is become the head of the corner.”

For the facts of the introduction of inoculation for

smallpox by a brave woman, Lady Mary Wortley Montagu, it suffices to quote from one of her own letters :

“I am patriot enough to take pains to bring this useful invention into fashion in England ; and I should not fail to write to some of our doctors very particularly about it, if I knew any one of them that I thought had virtue enough to destroy such a considerable branch of their revenue for the good of mankind. But that distemper is too beneficial to them not to expose to all their resentment the hardy wight that should undertake to put an end to it. Perhaps, if I live to return, I may, however, have courage to war with them.

“The faculty rose in arms to a man, foretelling failure and the most disastrous consequences ; the clergy descanted from their pulpits on the impiety of thus seeking to take events out of the hand of Providence ; and the common people were taught to hoot at an unnatural mother who had risked the lives of her own children.”

Inoculation was, of course, superseded by vaccination, and Edward Jenner's paper announcing his discovery, one of the most beneficent of all time, was refused by the Royal Society.

A still more recent case is that of hypnotism or hypnotic suggestion for therapeutic purposes, which was so bitterly fought, it is interesting to note, by a former editor of the *British Medical Journal*, and which is still practically taboo in Great Britain, notwithstanding the fact that James Braid was a Manchester surgeon. In this connection the reader who refers to the issues of the *General Practitioner* which contain the first reports of the competent pancreatic treatment of cancer in Great Britain will find therein some recent records of the results of therapeutic suggestion—records which would not be worth

printing on the Continent, so commonplace would they be, but which in this country cannot even find publication in the "authoritative" medical journals.

And the latest development in therapeutics and pathology is no exception to the rule. Just as the battle for surgical anæsthesia was fought, against the surgeons, by one who was not a surgeon; just as it was left to a chemist to teach physicians the nature of infectious disease, and surgeons the nature of inflammation and the "surgical" fevers, so it was left to an embryologist to discover the nature of cancer and point to the natural means whereby it may be cured and can constantly be relieved.

All medical means of treating cancer having been found futile, its therapeutics had been entirely relegated to the surgeons, while the problem of its nature was, of course, the business of the pathologist, whose science concerns itself with the nature of disease in general and diseases in particular. There is no surgeon worth considering except him who is also a pathologist; the surgeon, as such, is obviously no more than a highly-trained and responsible artisan. Among the great surgeon-pathologists will always be counted Sir James Paget, one of the glories of English science. His insight enabled him to perceive, at a comparatively early date, that a cancer is an *imitation-tissue*; but this dictum, the truth of which will soon be recognized, has been too frequently ignored by his successors. Apart from this, the contributions of the surgeon-pathologists to this problem have been of scant importance, dealing rather with the manner in which the disease spreads than with its nature. Much more important than any work of the surgeons were the labors of the great pathologist, Rudolf Virchow, of Berlin, who taught us to describe and estimate all disease-processes

in terms of the cell. Malignant disease, in all its forms, is very evidently a problem in what Virchow calls "cellular pathology"; but, unfortunately, the efforts of his followers have been directed—exclusively directed, one may say—to the description of the various cell-forms found in various tumors, the dictum of Paget that cancer is an imitation-tissue being forgotten. This dictum involves, of course, the truth that the various appearances found in various tumors are essentially accidental and superficial. Lately, indeed, Ehrlich and others have shown by inoculation through successive mice that cancer and sarcoma—long supposed to be fundamentally distinct varieties of malignant tumor—may actually be converted one into the other.

Needless to say, the work of Pasteur seemed to offer hope of solving the cancer problem. The disease might be due to an infection by some germ or microbe, and scores of such have been "discovered," each in its turn to be discredited by further inquiry. There seemed to be a resemblance between the multiplication of cells in a malignant tumor and that which is known to occur in inflammations, which are commonly due to the influence of microbes, as we have already seen. In certain of the lower animals a kind of growth, not unlike a malignant tumor, was shown to be due to the presence of parasites called *coccidia*, and the phenomena of *coccidiosis*, as the disease is called, seemed to supply a link between those of ordinary inflammation and those of malignant growths.

Further, the supposed discovery of cancer germs has led to the making of *antitoxins* or *serums* credited with the power of curing the disease. Notable among these is the cancer serum of the Parisian surgeon, Doyen, but it has been proved a failure. The bacteriologists, we may

say, scarcely count among the powers that be—or were—in regard to cancer.

These powers are the surgeons, the pathologists in general, and those workers specially employed by two or three bodies in this country, and by others elsewhere, for the prosecution of work at the problem.

The general attitude of the surgeons may be easily described. Rightly enough, as it seemed, they insisted that the one remedy for cancer is early operation, and they deplored all other methods as tending to lead to waste of priceless time. They were able to show that, when they were given the best chance, they could, on rare occasions, perform radical cures of true cancers, and, after long and varied collision with other methods of treatment, the vast majority of which were originated and prosecuted as means of making money, the surgeons might well be excused, until a comparatively recent date, for adopting a consistently contemptuous attitude toward all means of treatment other than the knife.

The pathologists in general, and the instituted researchers, continued to study the disease along the usual lines, describing the microscopic characters of various tumors, collecting statistics, and so forth. One notable advance, that might in time have led haphazard to the truth, was made by Professor Rudolf Jensen, of Copenhagen, who succeeded in inoculating mice with portions of cancerous tumors which had originated in other mice of the same species. The discovery of this possibility offered a wide field for experiment, the inoculated tumors being observed and their behavior noted. This it was, as we have seen, that led to the remarkable recognition of the possibility of transforming one kind of malignant tumor into another, hitherto supposed to be unchangeably different.

This discovery is of interest because of its entire consonance with the theory of Dr. Beard, which sweeps aside all the superficial differences between malignant tumors, over which the pathologists have wasted so many decades, and declares their fundamental identity. All the differences are mere masquerade, and nothing more.

Also, the observation that a mouse cancer cannot be inoculated successfully into a dog, or into a rat, or even into any mouse but one of the same species, if not of the same *variety*, is of interest because it consorts entirely with the theory of Dr. Beard. Apart from that theory it was a striking fact, but it had not led any one to the truth—*i.e.* the trophoblastic theory—which was, indeed, published by Dr. Beard long before the discovery that cancer could be inoculated at all.

So much for what the powers that were had accomplished. There was a large mass of work, the significance of which can now be appreciated, but all the workers were groping in the dark. None of them had the key, all were on wrong tracks. Hypothesis is invaluable in science, as Bacon did not recognize in his *Novum Organum*, but as has been abundantly recognized since his day. The powers that were had either no hypothesis, or wrong ones, and, if the past history of science is any guide, they might have continued to collect facts until the "last syllable of recorded time," without arriving any nearer to the truth. Your Dalton or Newton or Copernicus or Darwin or Pasteur is not only an observer: he has a creative mind. His scientific imagination provides him (it is always *him*, never *them*) with an idea, a true hypothesis, and *with this clue* he sets to work to collect the facts which ultimately establish his triumph. When a scientific committee, such as that of the Imperial Cancer

Research Fund, informs us that, in its study of a subject, it is studiously avoiding all hypotheses—adding a sneer at those who do not do likewise—we may be quite sure that it will accomplish nothing, or nothing but the accumulation of an unassorted heap of bricks, which is not the same thing as architecture. And no matter how sound and large and many the bricks, they will never *arrange themselves* into a tower foursquare to all the winds that blow. That is an act of mind, and of mind alone.

So when Dr. Beard had the temerity to advance the hypothesis of the trophoblastic nature of cancer, suggested by embryological facts known only to him and to the very few specialists who had studied his monographs of the past twenty years, the powers that were—and are not—were as indignant and obstructive as such powers have always been since the beginning, and will be until men learn that there is no authority but truth. What on earth could a complete outsider know about cancer? He had never seen a case of the disease, and had not even had a complete medical training. He was “not even a medical man,” said a prominent scientific journal, which might be thought to have heard of Pasteur. He was a biologist, and it no more occurred to the powers that were, and soon will be no more, that the problem of cancer might be a biological problem, than it occurred to their predecessors that inflammation might be a bacteriological problem. This matter was best left to those who had spent their lives in its study, who saw and handled and excised and made sections of cancers every day.

Dr. Beard's theory might be plausible enough—but he

had "no evidence." The truth, of course, was that he had abundance of evidence for a man of his knowledge and genius, but it was of a kind which the established powers had no means of estimating. It would have taken them a long time even to acquire an acquaintance with the necessary terminology. That not one surgeon in ten thousand should ever have heard of trophoblast is not in the least remarkable or disgraceful: the surgeon who undertook a systematic study of embryology could not be as good a surgeon as one who stuck to his last. But what adjective shall be applied to condemnation without understanding?

When the practicing physician or surgeon uses the phrase "no evidence," he usually means "no clinical evidence." To him it is the same thing: but it is not the same thing. And obviously there could be no clinical evidence until the matter had been put to a clinical test; and this was impossible until Dr. Beard had gained the help of some one with clinical opportunities. "Not even a medical man" himself, he could not adopt the obvious means of treating a patient or patients with trypsin, and publishing the results. He could only state his theory with the embryological evidence which, being published in medical papers, not read by embryologists, probably not a single one of all his readers ever appreciated—any more than, for instance, the present writer did.

Though I was myself a pupil of Dr. Beard's, and had read two of his monographs while I was a student, I cannot for a moment pretend that his views had ever specially gained my attention, deeply interested though I was in the problem of cancer. For me, as for every one not at once an embryologist and a student of Dr. Beard's contributions to that science, there was "no evi-

dence." But the case was changed when he published, in the *British Medical Journal* for January 20, 1906, his brief preliminary note on "The Action of Trypsin on the Living Cells of Jensen's Mouse Tumor." That was published, as usual, on the Friday preceding the Saturday which gave its date to the number of the journal in question, and I read it with bated breath on that day, In the evening, as I perhaps may be excused for recalling, I went to hear Prof. J. J. Thomson deliver one of his wonderful Friday evening discourses at the Royal Institution, and I can well remember, on leaving the famous theater, my amazement at realizing that I, an inveterate lecture lover, deeply interested in the lecturer and his subject, and accustomed to listen assiduously on such occasions, could not recall one single statement or conjure up the picture of one single experiment—if statements and experiments there were, as I should not care to deny.

Could there be some flaw in the work? The cancer was certainly deadly, for it was known to have killed thousands of mice. Both Dr. Beard himself, and the gentleman who, holding a vivisection license, made the inoculations, were known to me personally: it was impossible to question their good faith. The untreated mice had died. The tumors in the treated mice were actively growing when the injection of trypsin was begun. The remedy was not chosen haphazard, but was indicated by a theory of singular simplicity and completeness. Microscopic examination of the tumor-remains in the case of the treated mice confirmed the clinical evidence. That the treated mice lived and the others died was an observation not of a kind that admitted difference of opinion, or could be explained away as due to

the lively faith of a sanguine experimenter. If mice, why not men? Trypsin one had heard of in physiological classes as the most powerful ferment of proteid food-stuffs and as the chief product of the normal pancreas. Doctors had given it to their patients in the form of *liquor pancreaticus*, pancreatic powders and so on, for many years. Had the problem of cancer been solved? With such thoughts surging and resurging through one's head, even the corpuscular theory of matter, expounded by its author, could scarcely expect a hearing.

Plainly one had to do what doubtless all the surgeons were doing—write to Dr. Beard and obtain access to his previous contributions to the subject. The experiments were to be repeated and amplified by him, and of course they would furnish work for all the workers at the subject for some time to come; but meanwhile one must at least look into the basis of a theory that had led to experimental results so sensational and apparently so significant. Naturally enough, it was not long before I referred to Dr. Beard's work in the "Scientific Notes" which I contribute to the *Pall Mall Gazette*, and my comments appeared there on the 9th of February, 1906. Those notes had their result in a case or two, and greatly prolonged at least one valuable life. But otherwise *nothing happened*. There were no leading articles in the medical papers, and little or no correspondence on the subject. Apparently every one of the readers of the 25,000 copies or so that are printed of each number of the *British Medical Journal* had accidentally turned over two pages instead of one just at that place.

Further inquiry into the literature of the subject seemed to show clearly enough that Dr. Beard was on the right track. There was something that promised well

in the mere fact that all his work was so entirely unrelated to all previous work at the subject—the failure of which all the world knew. Therefore it appeared desirable to insure that an American hearing should be obtained for his views without delay, this being a matter of life and death; and an article of mine on the subject was published in *Harper's Weekly* for March 3, where I knew that it would reach a large audience, including, as my previous experience had shown, not a few capable of taking not only a serious but also an active and effective interest in any subject that seemed worthy of it. Only a week or two later, Prof. Morton of New York, in consultation with Dr. Beard himself, and with Messrs. Fairchild Bros. & Foster of that city, long known as the chief students of the ferments and their ways, began his series of trials.

There was everything in Dr. Beard's favor except the one damning fact that he was not one of the powers that be. Had he been an official and paid researcher, authorized by his appointment to frame hypotheses or conduct experiments regarding cancer, his results could scarcely have failed to receive as much attention as the official digest of sterile statistics or what not. On the other hand, he had published all he knew in scientific organs of the highest repute. His own record was known to all, and his status as an embryologist in one of the greatest medical schools in the world. He had no secret, no practice to augment, no fees to receive, nothing but honor or dishonor, according as he was right or wrong; and he had burned his boats, like his mighty peers before him. Only he was not a pathologist, nor a surgeon, "not even a medical man," or the holder of a medical degree; and his work had been done on his own dining-room

table in his spare time, and with material and a microscope which he had not taken the precaution of having paid for by a fund. He was just a servant of Truth, in her pay alone, his reward the hope or the realization of finding her. In a word, he was not one of the powers that be.

These, then, fell upon him. They began by publishing in the *British Medical Journal* a statement to the effect that he had not had their permission to describe his experiments as having been conducted—as they were—in the laboratory of the Royal College of Surgeons of Edinburgh. (They had to be conducted there, owing to the occurrence of so-called “vivisection” in their first stage.) For the rest they ignored him. Without their help his proposed treatment could be applied to no human cases. In the course of ten months some thirty doctors in all in Great Britain wrote to him concerning this subject. Among them was *not one* writing as the official representative of any cancer hospital or any hospital at all. We may observe that in this country some thirty thousand persons die of cancer every year. Still, thirty doctors did write to Dr. Beard—one for every thousand deaths from cancer *per annum*.

Week by week the medical papers in this country appeared without any record of cases treated by trypsin. Successful results would obviously have been important: no less important, though in another fashion, would have been unsuccessful results. None appeared, successful or unsuccessful, though week followed week and month followed month. So early as August of last year I could have published in the *Fortnightly Review* an article which the editor so far honored me with his confidence as to promise to print. But though I had myself seen astound-

ing things in a case at Leytonstone, treated with scrupulous and admirable skill by Dr. Bonnefin, I did not dare. The responsibility seemed too great, and my courage failed me, as I deeply regret to admit. The only excuse can be that there was then no clinical evidence of such a kind and extent as adequately to support the theory; and the kind of evidence upon which it was based could not have been properly presented within the limits of a review article. So I delayed, doubtless thereby earning wholly undeserved credit for the exhibition of "scientific caution," which is occasionally what it purports to be, but is more often cowardice, or stupidity, or both. Meanwhile I heard from Prof. Morton that he was *getting results*.

Then Prof. Morton sent me an advance copy of his report, which appeared a few days later in the *New York Medical Record* for December 8, 1906. A case of cure had been reported in the same journal a fortnight before, and in the issue which was to contain Prof. Morton's results other results were also to appear. I cast to the winds the so-called "caution" which I have already more truthfully described, and published a signed discussion of the matter in the *Pall Mall Gazette* for December 10. Perhaps one of the most noteworthy facts that almost immediately followed was the receipt of courteous letters from the respective editors of notable reviews on both sides of the Atlantic—*after* the publication of Prof. Morton's report, be it remembered—in which each referred to an unnamed adviser who was looking closely into the matter for him, and had advised him not to publish my article, which in each case had been accepted beforehand, and in one case had even been paid for. Now these two gentlemen, as we now see, knew nothing about the sub-

ject. But they were actually prepared to take, and did take, the grave responsibility of arresting the publication of statements which might, at any rate, lead to the saving of valuable human lives. Doubtless their advice, being followed, did affect the consignment to the tomb of not a few who might be alive and well, or at least comfortable, to-day, but who were consequently left to their horrible fate. When they gave their advice, the cases of Dr. Rice, Prof. Morton, Dr. Cleaves, and Dr. Golley—amounting to thirty-four in all—had already been published. It is scarcely credible that, giving such advice, they had acquainted themselves with the records of these cases; and if they dared to give such advice without doing so, what decent word shall be spoken of them?

The subsequent behavior of the powers that be may conveniently be discussed under various headings, and we may begin with the medical press in Great Britain. Dr. Beard being an Englishman, working in Great Britain, it was, of course, in the prophet's own country that these facts were observed. Until this present I have made no reply, except in the recent *Observer* letter, to any attacks in the medical press, it being more convenient to defer brushing the mud off one's clothes until it is dry. I write now without any grudge against individuals, since I am happily unacquainted with the names of all but one of the writers to whom I shall refer. My quarrel is with institutions.

A paper called *The Medical Press and Circular*, the motto of which is "Salus Populi Suprema Lex," conformed to that great principle by publishing (December 19, 1906) as its leading article an insolent attack upon myself, observing that practitioners were in no need of Dr. Saleeby's help on this subject, "having acquired their

information where that writer has presumably failed to look for his, namely, the current issues of medical periodicals and recently published books on the subject," and that "the hollowness and futility of the whole business was exposed by interviews with cancer hospital authorities, by which it was revealed that trypsin had been tried both at the Middlesex Hospital and at the Cancer Hospital, and had proved disappointing in their hands." We know now what manner of fatal farce these trials were. The writer of this leading article—leading all who believed it on the road to death—warmed to his work, and concluded his exhibition of audacious and maleficent ignorance by asking me for an "ample apology." It is something to have genius, if it be only a genius for effrontery. Properly, apology means defense, and as this book constitutes, among other things, a defense of my action in this matter, I submit it to the *Medical Press and Circular* as the "ample apology" for which it asked.

On March 20, 1907, the same journal took the opportunity furnished by an article published in New York in criticism of *one* case of Prof. Morton's twenty-nine to say that the evidence on which I relied for my "extravagant statements was easily seen to be insufficient, and in the light of further information has vanished altogether." The last two words, monstrously untrue, lead me to hope that the writer was also the writer of the previous article. One such contributor is enough for any paper. Such, at any rate, was the contribution of this journal to that safety of the people which it regards as the supreme law. One wonders how many patients were killed by cancer whom its readers were dissuaded from treating by the pancreatic ferments.

I have referred elsewhere to the ignorance which has

prevented our critics in any instance in all this time from advancing the excellent argument as to the (supposed) development of anti-trypsin. Here I may briefly note the following sentence taken from the *Medical Press and Circular's* review of Dr. Shaw-Mackenzie's book, elsewhere referred to: "How many physicians and surgeons *e.g.* ever heard of trypsin before the author . . . proved its therapeutic value, besides showing its action on glycogen?"¹ As we have seen elsewhere, no one whose knowledge of the ferments could cover a visiting-card could possibly imagine that trypsin had any action on glycogen. This is the kind of knowledge which has set itself to criticise Dr. Beard, and with this citation the *Medical Press and Circular* may be dismissed. I will not ask it for an "ample apology," but I will watch its future attitude on this matter with deep interest, and will discuss it at my convenience.²

The most prominent of our medical monthlies is the *Practitioner*. In its issue of February, 1907 (p. 289), this paper printed an editorial article which said, speaking of trypsin: "To vaunt it as a cure before anything at all like a cure has been achieved is a crime against mankind." This three months after the various American reports had been printed. The reader will judge as to who, in this matter, have been guilty of a "crime against mankind." The article also contains various remarks about Dr. Beard, which suggested to me the quotation from Robert Browning that stands at the head of

¹This absurd sentence is still being quoted in advertisements both in the *Medical Press and Circular* and the *British Medical Journal*.

²Meanwhile its publication of a favorable case (Oct. 2, 1907) may be welcomed.

this chapter. The writer, palpably as ignorant of the elements of the subject as the table on which I write, referred to Dr. Beard as a "highly scientific person" and a "cancer crank." Since Dr. Beard is not a medical man, and has received no fee from any one for his prompt and priceless and unfailing advice in numberless cases, he could not be described as a "cancer quack," but the nearest phrase to that was employed. Not that many cancer quacks, many of them with high "qualifications," have not abounded in this business. Those who have written and promulgated all the malignant nonsense which has delayed the control of this malignant disease for nearly two years past have earned the title of cancer quacks a thousandfold more abundantly than the fools and knaves without "qualifications" or degrees who have been so stigmatized in the past.

Nature is not a medical journal, but the leading scientific journal in this country. It published (December 20, 1906) an adverse comment on my *Pall Mall Gazette* article, and in its reply to the letter which its remarks drew from Dr. Beard stated that "the pancreatic enzymes must be injected into the neighborhood of the growth or used locally; how, then, could the secondary growths in internal organs be attacked? Until this can be done, no cure for cancer will have been obtained." Dr. Beard's second letter, correcting this most important and inexcusable error, was not inserted, and the statement was allowed to stand.

The *Hospital* (January 26, 1907) reproved me for my *Pall Mall Gazette* article. It said, of Prof. Morton's report, "even on the most sanguine view of the cases one fails to find any justification for the enthusiasm with which the so-called 'cure' was proclaimed by Dr. Saleeby

in the lay press." I wonder what the writer now thinks of that word "any" in this extract. On April 13, 1907, the *Hospital* reviewed a number of volumes of the *New Library of Medicine*, of which I am the editor. Its remarks were exceedingly generous to myself, showing that no animosity against me was present, but not so with the pancreatic treatment of cancer. The series includes a volume written by a well-known surgeon at my request—made before Dr. Beard's experiments were published—to show the public that the surgeon could sometimes cure cancer if only he were called in early enough. My hope was thus to accomplish in Britain the useful work of education begun in Germany. The reviewer says that the author "shows the failure of the many so-called cures—Christian science, X-rays, high frequency currents, cancroin, violet leaves, molasses, trypsin," etc. Note the conjunction of molasses and trypsin. Now it need hardly be said that I could not permit any assertion of the failure of trypsin to appear in a book under my editorship, even had the author made such an assertion, which he did not. There is no syllable in the book anywhere which offers a shadow of excuse for this misstatement, by which it was made to appear that I, the only public advocate of Dr. Beard, had abandoned my belief in his method. On the contrary, the volume contained the best account of the trustees and the Moray Research Fund of the University merely observed that, if the theory were accepted, it only confirmed his argument as to the local origin of cancer.

I am merely selecting a few specimens from the host which might be quoted, it being necessary to place the attitude of the medical press on record, partly in order to explain the reception of the new treatment and partly for its general sociological interest and its relevance to

the age-long struggle between authority and originality in all spheres of human activity. But I do not mean to burden my pages with more than will suffice for these necessary purposes. In dealing with the *Lancet*, the most celebrated medical paper in this country, I shall content myself with one abundant fact. On February 4, 1905, the *Lancet* published a paper by Dr. Beard, entitled "The Cancer Problem." This was an abstract of the paper read by him before the Edinburgh Pathological Club on December 13, 1904, a date which may be remembered down the years, and containing the first statement of the theory that the pancreatic ferment trypsin should afford a means of opposing the growth of cancer. In 1902 Dr. Beard had declared that cancer is "irresponsible trophoblast," and in this paper, two and a half years later, he completed his work.

The *Lancet* discussed this memorable paper in its leading article, from which I make the following extracts:—

"We publish to-day a paper on cancer by Dr. John Beard, lecturer on comparative embryology in the University of Edinburgh, which is the third of a series that has appeared in our columns. The writer states that it is based on work carried out with the support of the ample funds³ for research at the disposal of the Carnegie trustees and the Moray Research Fund of the University of Edinburgh. We have thought it well to find space for this paper, for it seems to us to be a serious matter that it has been produced with the countenance of the wealthiest endowment for research in this country. The present contribution is itself the best commentary and criticism upon the two previous articles, and its character

³A few shillings of these "ample funds" were all that Dr. Beard expended.

makes it incumbent upon us to state clearly the illogical reasoning upon which Dr. Beard's conclusions are based, seeing that they have already received qualified acceptance from some pathologists who probably would not subscribe to a bald statement of the fundamental conceptions upon which a fantastic but seemingly logical superstructure has been raised. . . .

"In short, Dr. Beard passes from one conjecture to another. He begins by views on embryology which on his own showing are not generally accepted by embryologists. He goes on to express opinions on the histology and the pathology of cancer which are not in accordance with known truths, and launches into the realm of therapeutics with assertions about the action of ferments which would inevitably cause the rejection of a candidate in physiology. We are anxious to encourage the serious biological investigation of cancer, and we trust that we are doing so by eliminating from the hypotheses worthy of future consideration one characterized by more wild speculations in more fields of knowledge than any other with which we are acquainted. In the present chaotic state of the cancer problem there is much preliminary clearing up to be done, and we can only regret that our opinions on the nature of those biological investigations of cancer which are worthy of financial support differ so essentially from those entertained apparently by the Carnegie trustees and the Moray Research Fund of the University of Edinburgh. In estimating the value of contributions such as that which we publish to-day, much larger issues are raised than the mere scientific value of the paper itself. By the indiscriminate distribution of funds for research purposes, proper support may be diverted from more important research in the true sense

of the word, and the question of the competence and the responsibilities of those administering funds for research purposes may obtain a prominence unfavorable to the reputation of British scientific medicine."

This article is none other than a scurrilous personal attack on Dr. Beard. The *Lancet* turned to its lasting dishonor an occasion which would otherwise have redounded to its lasting honor. It printed the paper, as the writer says, only in order to discredit it. The identity of the writer is, of course, unknown. He is protected by the anonymity which has been the disgraceful defense of nearly every one who, during the past two years or so, has fought against the new treatment. There is internal evidence, and other evidence, which makes it certain that the writer was himself a cancer researcher, and highly probable that he was the most prominent among such workers in Great Britain at the time. Whoever he was, he may here be dismissed with a gesture of disgust.

We must now proceed to the case of the *British Medical Journal*, to which special sociological importance attaches. This is the official journal of the medical profession in Great Britain, in that it is the official journal of the British Medical Association. No other journal in this country speaks with nearly so much authority; none other has so much power. It has an enormous circulation within the profession and a very large circulation outside it. It is pre-eminently the type, then, of an established and official power, and its attitude in this matter may well be studied by any student of the principles of progress as a test case in determining the relation of authoritative and established institutions towards the pioneer. We shall have to decide whether in this matter

it has acted as the Church in the case of Savonarola, the Royal Academy in the case of M. Rodin, the University of Oxford in the case of Locke, the Italian universities in the case of Galileo, and, in short, all established institutions of whatever kind in all times and places.

Just as the *Lancet* was honored by publishing the first statement of the only substantial discovery regarding cancer that has ever been made, so was the *British Medical Journal* honored, as we have seen, by publishing, on January 20, 1906, the result of the first experiments in confirmation of that discovery. This was printed without comment, though it is evident that critical comment based upon knowledge would have been invaluable at such a juncture, and that abundant opportunity for such comment was afforded. Shortly afterward the journal published a "special cancer number" which took no note of the new work, while the corresponding journal in America (*Journal of the American Medical Association*), which is not the prophet's own country, did afford a certain amount of space to the subject after the publication of my first article in *Harper's Weekly*. None was afforded it in the *British Medical Journal*. This passive resistance, however, assumed an active form on the publication of my article in the *Pall Mall Gazette* on December 10, 1906, in which, having received from Prof. Morton an advance copy of his report of December 8, I published his main conclusions. On December 15 the *British Medical Journal* published an article censuring me. I have refrained from any reply to the journal until this present because I was aware of the fashion in which Dr. Beard's letters were treated by the suppression of one sentence and the insertion of another. By such methods it is possible to make your opponent assert that which he denies, and

conversely, and there is no remedy. Thus my present mode of reply is more convenient. The article I refer to should really be read in full. I have no taste for noisome dissection, and will not discuss it further. In the following week there was a second article of the same quality as the first.

The journal publishes every week an epitome of important communications to the medical press abroad. As month followed month it published only an account of Prof. Morton's report, which I had made it impossible to ignore, of a report of failure by an incompetent American practitioner whom I need not name, and of Dr. Rice's case. The attention of the readers of its epitome was not drawn to a single one of the successful results which were recorded in the American medical press from January, 1907, onward, though the journals were of the highest repute, and though week by week the epitome included accounts of other communications to those same journals. The work of the *British Medical Journal*, however, consisted in the publication of a highly adverse article on January 19; yet another (January 26), on an address delivered by the general superintendent of the Imperial Cancer Research Fund, and then on March 2 a triumphant article, accompanying a critical paper in which a single one of Dr. Morton's twenty-nine cases was further discussed. This case did not maintain its improvement, and the growth recurred after the operation. This active recurrence after operation was taken as evidence against trypsin, whereas, of course, it was really evidence against the knife. Elsewhere I discuss Von Leyden's principle of the reaction of malignant tissue to mechanical injury.

From December, onward, I waited impatiently for several months before returning to the attack, meanwhile

having my belief in Dr. Beard confirmed by the cases I was myself observing, in company with my friend, Dr. Meggitt, who was responsible for them. These patients owed the incalculable benefits they received not to the medical press, but to the *Pall Mall Gazette*. There then appeared Prof. Von Leyden's confirmation of Dr. Beard's main thesis, that trypsin has a specific, digestive and toxic action upon living malignant cells. Armed with this and other evidence, I wrote a further article in the *Daily Chronicle* (May 18, 1907), described as "by a student," and a series of eight articles in the *Daily Mail*, beginning May 29, described as "from a special correspondent." To these the *British Medical Journal* replied in an article of June 15, entitled "Another Cancer Boom." The writer asks, "But how on earth is the medical profession to study seriously cases that are not reported," and declared that the *British Medical Journal* "has impartially published reports of all the cases that have come within its ken. We have further carefully analyzed the clinical evidence appealed to by the supporters of the new method. We have not, however, been so fortunate as to find a single case of cure, even in the limited sense in which that word is used by surgeons." In this article the name of Prof. Von Leyden and his work were not mentioned. This is to say that, even in the face of the *Daily Mail* articles, the journal took upon itself the responsibility of continuing to suppress, in so far as was possible, the authoritative German confirmation by the chief living authority on cancer in the whole world, and to deny the existence of, for instance, the two cases reported cured by Prof. Morton in December, though these had been epitomized in its own columns, not to mention many other cases, some of which are elsewhere referred

to. The writer then proceeds to say that the writer of the *Daily Mail* articles "cites as examples of cure cases that have been publicly shown to be nothing of the kind." This is an absolutely inexcusable rendering of the fact that *one* of Prof. Morton's twenty-nine cases had been criticized successfully, as I admit. No other case, either of Prof. Morton or any one else, had been publicly criticized anywhere; nor had I cited this as an example of cure. The writer then goes on to say that "Prof. Morton's cases are again trotted out, and it is said that he had already obtained 'two absolute cures' when he wrote, 'while in every case, without exception, the patient was benefited.' This is simply untrue." I have no words for this indescribable statement, which simply consists in giving the lie to Prof. Morton, who did actually in his report of December 8 state that two cases had been cured, and that "in all cases signs of amelioration in the progress of the disease have been observed."

Then the *British Medical Journal* proceeded to excel itself. It said: "Prof. Morton has since published a series of cases of cancer treated by another method, and this at least suggests that his faith in the pancreatic treatment is perhaps a little shaken." I wrote at once to Prof. Morton and ascertained the facts, which I here put on permanent record: In the first place, he had published in the *New York Medical Journal*, March 9, 1907, a new case in which the treatment had been absolutely successful. This case was not reported by the *British Medical Journal* in its epitome. As for the "series of cases treated by another method," the fact is that this was merely a paper on the X-ray treatment of cancer, which had been originally read by Prof. Morton in May, 1906, a few days after his attention had first been directed to trypsin. In

his letter (June 31) to me Prof. Morton describes the statement of the *British Medical Journal* in terms too contemptuous for me to reproduce. In that letter he also says, "I have published no cases of cancer treated by any other method since my trypsin series of cases, nor is my faith in the pancreatic treatment in the least shaken—on the contrary, it has steadily grown."

The article concludes by saying: "With Dr. Beard's theory we are not here concerned; it is the practical result that interests us. What that has been so far we leave our readers to judge." We have observed in what manner the journal attempted to assist the judgment of its readers. The next statement is that it is foolish to suggest that the new treatment may be a serious matter financially to the surgeons, since "the profession can only gain by any increase of its resources against disease." Now I will not go so far as to say, as has been said, that the surgeon's prayer is, "Give me this day my daily tumor"; but if any one will maintain that, let us say, the elimination of cancer from the sphere of surgery would be a matter of financial gain to surgeons, I am content to leave him to the refutation of universal laughter. The last sentence of this article, referring to a genuine cure for cancer, says, "Unhappily, we see no sign that it has yet come." Perhaps the one form of blindness which no science will ever cure is that of those who will not see. The omission of any reference to Von Leyden's work was a piece of daring which astonished me, but we were to find in a short time that, though his work was not mentioned, the *Daily Mail* references were attended to.

In my judgment, the article I have cursorily analyzed touches the nadir of controversy. I am happy to say

that it was the last but one of its kind. The tide had to turn at last.

In the next four issues of the *British Medical Journal* there was abundant opportunity for yet more blows at trypsin. For instance, the journal published (July 6, 1907) the highly important report of the Imperial Cancer Research Fund Committee, which condemned trypsin as without action on cancer. This conclusion was put into the mouth of H. R. H. the Prince of Wales, and was quoted and commented upon everywhere. To my absolute astonishment, the journal published the report, not merely without a leading article on the subject, but without even an editorial paragraph. I say absolute astonishment, because in the face of the fact that Prof. Von Leyden's confirmation of Dr. Beard had been ignored for months, I had begun to persuade myself, I suppose, that the *British Medical Journal* would brazen out its opposition to trypsin to the end of time. In the following week the journal might have been expected to reply to Dr. Beard's fierce indictment, printed under his name, in the *Observer* of July 7. No allusion was made to this, however. The case was explained in the succeeding issue—that of July 20. Here, also, there was no reference to the *Observer* discussion, which was still continuing.

But there was something else, and if any one is unacquainted with the meaning of the word disingenuous, I submit to his notice the leading article of July 20, 1907, entitled "The Pathogenesis of Malignant Tumors." The writer discussed, for the first time, the work of Von Leyden with the liver-ferment, and admitted Von Leyden's demonstration of the specific action of trypsin on cancer—indirectly, in a fashion I will show. No reference was given to the most important paper in the *Zeit-*

schrift für klinische Medizin, and no allusion to that paper has yet been made in the journal, though it has, of course, been epitomized in the *Journal of the American Medical Association*, and was prominently noticed in France.

The nature of this paper was commented upon—not by me—in the *Daily Chronicle*, drawing a reply from the journal (July 27, 1907). This reply, besides much irrelevant humor of sorts, and a complete avoidance of the question at issue, contains this remark of the treatment: "What we ask for are some authentic facts in proof of its practical value." I will show that the facts recorded abroad had been systematically suppressed by the journal; and even when Dr. Beard, in writing to it, gave the reference to a noteworthy report, published in the *Journal of the American Medical Association*, the paragraph containing the reference was omitted from Dr. Beard's letter as printed.

I had already asked the editor of the *Observer* to send an interviewer to me, and my remarks appeared in that paper on July 14. I did not give my name—following the policy pursued in the *Daily Mail*, the *Daily Chronicle*, and the *Morning Post*, since, constituting an army of one, I had to adopt the obvious stage device, and since I did not want to make possible the argument that this was only Dr. Saleeby again. But on the publication of the latest article in the *British Medical Journal* I sent a signed letter to the *Observer*, the greater part of which was printed on July 28, 1907, under the headings, "Burking the Trypsin Treatment: Why English Research Has Failed." The headings for the interview were, "Strong Indictment: Why England Lags Behind." I here print my letter as it appeared. I followed it the next week by a brief note of some recent references.

“Your readers and the public are much indebted to you for taking up the question of Dr. Beard’s work on cancer. The recent report of the Imperial Cancer Research Fund Committee, condemning trypsin as without action on cancer—an opinion which was put into the mouth of H. R. H. the Prince of Wales, and has been quoted everywhere—contains no statement of the evidence for this opinion, which is merely of the ‘because I say so’ order, and has no relation to what is known as science. As your readers are aware, the committee was long ago challenged by Dr. Beard to state the details of their experimental methods, and that challenge was declined. The time is not ripe for a scientific report, we are told; but the time was not thought unripe for the broadcast assertion, without evidence, of a statement which is now merely ridiculous.

“It may be remembered that I recently discussed, at length, the work of Prof. Von Leyden, noting his definite and mature conclusion that trypsin has a specific toxic action upon malignant tissues. In criticizing those articles and the remarks of the *Observer*, the *British Medical Journal* made no allusion to Von Leyden nor his work, which had been entirely ignored in its columns. But it became evident to me that the tide was about to turn, when, to my astonishment, I found that the *British Medical Journal*, publishing the report of the I. C. R. F. committee, made no editorial comment thereon. This was of some interest, since the journal has hitherto missed no opportunity of writing in opposition to trypsin.

“A writer in that journal made attempts to weaken the case for trypsin by saying that Prof. Morton, the first American physician to act on Dr. Beard’s teaching, has published, since his favorable report of last December, a report of cases of cancer treated by another method, ‘and this at least suggests that his faith in the pancreatic treatment is perhaps a little shaken.’ I have an indignant letter from Prof. Morton commenting on this. I will not quote his contemptuous characterization of it, but will merely observe that our anonymous writer omitted to

note that the paper in question is merely a paper on the X-ray treatment of cancer which was read by Professor Morton, in May, 1906, a few days after his attention had first been directed to trypsin. I submit that the appropriate comments on a style of controversy which descends to such methods will spontaneously occur to the reader, and I may pass on. Merely I will note that Prof. Morton has published, since his first report, a further successful case—which has been absolutely ignored by the *British Medical Journal*, and that, in his letter to me (June 31), he says: 'I have published no cases of cancer treatment by any other method since my trypsin series of cases, nor is my faith in the pancreatic treatment in the least shaken; on the contrary, it has steadily grown.'

"But there is something else. It is a leading article, entitled 'The Pathogenesis of Cancer,' and in it the readers of the journal are introduced in a curiously imperfect fashion to the work of Von Leyden. The greatest part of the article is devoted to Von Leyden's newest work on the use of a liver-ferment in cancer. There is no mention of Dr. Beard, no word of trypsin. This ferment is judiciously referred to as 'pancreatin,' or, most amusingly, as 'the pancreatic ferment.' There are at least four pancreatic ferments, but the simple word trypsin was taboo, like Dr. Beard's name. However, the specific digestive action of 'pancreatin' upon malignant tissue is acknowledged for the first time in any leading medical journal in this country.

"I suggest that the puerile and inaccurate subtlety of calling trypsin the 'pancreatic ferment' be discarded, and that the readers of the official journal of the medical profession be informed frankly, and not in the fashion of the article I refer to, that, in spite of the ignorant abuse to which Dr. Beard and myself have been subjected in its pages on every possible occasion, Dr. Beard's magnificent theory of the specific destructive action of (active) trypsin on malignant tissue (first stated on December 13, 1904) has been conclusively confirmed by the world-famous experts of the Cancer Research Institute of Ber-

lin, and that from America and Italy and Germany have already come a number of detailed, responsible and independent reports which demonstrate the magnificently successful application of this fact to the rescue of victims of cancer.

“If patients can be saved in America—and now not in America only—why not here also? In point of fact, a few patients are being saved here, patients whom surgery has abandoned and who have no hope but this in the world. I myself, though I do not practice medicine for fees, am watching, and have long been watching, such cases in consultation with the physician in charge. Nothing has been published, because it seemed useless to seek publication in the face of the attitude of the medical press and the Imperial Cancer Research Fund; but the tide has now turned, and we shall publish soon. Meanwhile many patients, abandoned by the surgeons who can do no more for them, and almost persuaded to undergo the treatment (which involves no risk) by my various publications in the lay press, have, as I know, been dissuaded by the opinion—I will not abuse language by calling it a verdict—of the I. C. R. F. Committee, which must now be arousing curious reflections in New York and Berlin.”

To this letter, involving the most serious suggestions as to the honor of the official journal of the medical profession, charges made under the signature of a member of the British Medical Association, *no reply whatever was made*. This public and detailed and signed incrimination of the journal, accusing it of misrepresentation, of suppressing vital facts, and of ignorant abuse in place of argument, remains unanswered to this day, as does the interview with me, and Dr. Beard's *Observer* article and my *Contemporary Review* article. I suggest that no reply was made to accusations so dishonoring to the accused, if true, and to the accuser, if untrue, because there was no reply to make.

This discussion cannot disgust the reader more than it does me, and I have nearly done. Merely I note, however, that the journal has repeatedly asked for facts, and has declared that it has always noticed facts brought to its attention. It weekly publishes an epitome of the principal articles in the medical press elsewhere. During the present year it has published an epitome of one report on trypsin, found in a minor American organ, the *Boston Medical and Surgical Journal*. The reporter was obviously incompetent; his report was adverse; it was epitomized at great length. But no epitomes have appeared of the following reports, published during 1907, and I have already noted the deliberate suppression of the paragraph in a letter of Dr. Beard's which drew attention to one of them:

N. Y. Medical Record, Jan. 5, Feb. 2, June 1, July 6.

Journal A. M. A., Jan. 19.

N. Y. Medical Journal, Feb. 23, March 9.

New Orleans Medical and Surgical Journal, July.

Meanwhile neighboring articles from these same journals, the first three of which are the three leading medical publications in America, were epitomized. I state the fact and submit it for interpretation by the public and the grievously misled general practitioner. Lastly, I turn to Germany, and note the following papers, of which no notice whatever has been taken. In each of them the specific action of trypsin upon cancer is asserted:

E. Von Leyden: *Zeitschrift für klinische Medizin*, Vol. 61, pp. 360-365.

F. Blumenthal: *Ergebnisse der Exper. Pathol. und Therap.*, Vol. 1, Pt. 1, 1907, pp. 65-104.

Neuberg and Ascher: *Arbeiten a. d. Pathol. Institut zu Berlin*, 1906.

P. Bergell: *Zeitschrift für Krebsforschung*, Vol. 5, pp. 204-208.

Pinkuss and Pinkus: *Medizin. Klinik*, Nos. 28 and 29, 1907.

This is the fact of the behavior of the journal which almost weekly denied the existence of facts in this matter and desired to be informed of them.

It is a natural consequence of the action of this journal that neither at the British Medical Association Annual Meeting at Toronto in 1906, nor in Exeter in 1907, was any paper for or against the pancreatic or any other ferment treatment of cancer read or referred to.

It may be noted that the principal American journals can always be consulted in the reading room of the British Medical Association, and that a visitor, having read the demand for facts and cases to be studied, had only to stretch out a random hand without even leaving his seat to pick up in its own home the records of which the journal before him denied the existence. It is impossible to believe that any writer could pen a demand for records and deny their existence with his right hand, and drop them into the waste-paper basket or put them under cover with his left. This increases the probability that the writer in question sends in his contributions to the office from the outside. I do not know how it should come about that, being entrusted with the discussion of this subject for the most responsible medical journal in this country, he should be entirely unacquainted with its current literature, whether American or German. Still less do I understand why, failing to make himself acquainted with it, he should deny its existence. If trypsin were proved to-morrow to be a constant and deadly poison, it would still be impossible for the *British Medical Journal* to defend itself should it make a tardy attempt to do so. I find it impossible to believe the less charitable hypothesis, and so I must leave this point merely with a note of astonishment at the existence of such a person

as this unknown writer, not to mention his employment in any responsible quarter. I may note in passing that I am greatly indebted to the invaluable opportunities afforded by the reading room of the British Medical Association for the collection of favorable reports on the ferment treatment of cancer. It has been highly convenient to visit that comfortable room, gather up the evidence, and write my comments on the journal there.

Lastly, Dr. Francis Cavanagh, whose remarkable report I refer to elsewhere, has forwarded me some facts and documents with his permission to employ them as I think fit. He sent his report to the *British Medical Journal* on August 7, 1907. Three weeks later, August 28, he wrote commenting on the omission of any acknowledgment, either by post or in the journal, and stating that he intended to publish elsewhere. Thereupon his report and letter were acknowledged in a letter from the editor of the journal, who states that the cases are too incomplete for publication, that they are inconclusive, and that "in regard to the first case in particular there is no proof that the tumor was of a malignant nature." The curious reader will refer to Dr. Cavanagh's report for himself as to this.

My friend Dr. Cavanagh being a contributor to the *General Practitioner*, I was enabled to draw his attention to this matter, and in consequence that paper is the only medical publication of any note in this country that has not opposed the new treatment. I discuss its services in another chapter, and here note that the *British Medical Journal* has made no reply to its recent editorial article of September 7. Apart from this guidance the general practitioner, who has no time to read the foreign and American medical press, has throughout been completely

kept in the dark as to the results obtained and the work done in America and Germany, while of the few practitioners who have communicated with Dr. Beard or myself, many have not dared to seek publication of their results. Nothing could well be more remarkable—or, to the student of progress, less remarkable—than the contrast between the medical press in this country and that of America and Germany and France in this respect during the past two years. Let any one contrast and compare the files of the journals of the British Medical Association and the American Medical Association, respectively, and he will see the difference in the manner in which the two journals have influenced their readers. The American paper has not declared itself a believer in trypsin, but it has not published editorial articles against it, and has not suppressed all allusion to the (favorable) work done in America and Germany.

The reader will observe the behavior of the journal of the general practitioner, as against that of the journal which is in the hands of the specialists.

I pass now to another established institution which has exercised a most baneful influence upon progress, both in its own name and through the medical press and the surgeons. It was not the intention of those—much-to-be-honored surgeons and others—who founded and endowed the Imperial Cancer Research Fund to stifle cancer research. But he who founds a church, or an academy of painting or music, or any other institution, is in danger of injuring the very cause for which he works. An institution may perchance find a *man*, and he will possibly work as well within it as he would without, though even he runs great risks. Failing a *man*, however, posts must be filled, and mummies or mounte-

banks or mammon-worshippers may be installed, and then the church kills religion, the academy art, the research institute science. All history is open to the inspection of those who desire to see these principles illustrated.

Long ago the I. C. R. F. Committee declined to supply Dr. Beard with mice for his experiments. This and the host of similar facts in this chapter mean what they mean, whether or not trypsin is remedial in cancer. In the *Journal of the American Medical Association* stands the uncontradicted statement by an American physician that, during the Toronto meeting of the B. M. A. in 1906, Dr. Bashford, the director of the I. C. R. F., informed him, of trypsin, that "the Imperial Cancer Research Committee had given it a very thorough trial and had no good results to report from it." I have reason to believe that this "thorough trial" consisted of injections into one mouse, with a tumor nearly as large as itself, of a trypsin-preparation which is, or has been until lately, notoriously inert. No details whatever as to these experiments have ever been published, despite the repeated public challenges of Dr. Beard and myself, and I am willing to predict that they never will be.

I have already informed the reader as to the statement made in the report of the Committee for 1907. It cannot be criticised, in a sense, because no details as to the experiments are published, but that fact, of course, constitutes in itself a criticism which renders the report wholly irrelevant to any scientific inquiry.

It would be easy to show that during the five years of its existence the Committee has not hitherto distinguished itself. It has collected some statistics, published confirmations of other people's work, and then withdrawn

them, and has figured very largely in the public eye. The Committee is not to be blamed for having made no substantial addition of any kind to our knowledge of cancer: doubtless it did its best. But the public is entitled to ask why the published challenge of Dr. Beard, demanding the actual facts of the Committee's experiments, has been wholly ignored. Meanwhile the failure of these undescribed experiments was bruited everywhere in this country, and by a critic or two in America, as an authoritative verdict, while the public and the profession were and are kept wholly in ignorance of the fact that directly opposite conclusions have been published abroad by some of the greatest living experts, with full details of their methods and procedure, such as, of course, are inseparable from any serious scientific report. A mere *ex cathedrâ* statement may be repeated in good faith by the Prince of Wales and scores of newspapers; and it has the advantage of avoiding the criticisms which, if the details were made known, might show how, in one or in half a dozen respects, success was made impossible. I remind the reader, in passing, of a fact duly made known to the profession in America but ignored in Great Britain, that Dr. Beard's results in the mouse have long ago been confirmed in Italy by Dr. Zanoni.

It may be noted that abundant internal evidence suggests that, as is natural, the directors of the *British Medical Journal* have intrusted to some prominent cancer researchers the discussion of cancer in its columns. To the I. C. R. F. Committee, also, may probably be attributed the answer of Sir H. Campbell-Bannerman, in the House of Commons (June 27, 1907), to the question whether he would appoint a Royal Commission upon cancer. The Premier said that the best qualified authorities ad-

vised him that much remained to be done before such a Commission could be made of use.

This demand for a Royal Commission to inquire into the subject had already been made by me in the *Daily Mail*, and I here repeat it. I am happy also to draw attention to a long letter published in the *Morning Post*, April 16, 1907, and signed "F. R. C. S." The writer is unknown to me. He strongly demands the appointment of a Royal Commission, and says of the use of trypsin in cancer, "the uniformity of beneficial results has been remarkable," and "after some two and a half years of the practice of this method, it may with truth be said that a milestone in the roadway of the history of this distressing malady has been reached." I only wish the writer had the courage to publish a paper on the results he has observed.

As evidence of the results which followed the publication of the I. C. R. F. Committee's report, it will suffice to say that, having sent a most moderate article, containing all the available evidence, to my friend the editor of a leading review, I received a letter, dated August 6, 1907, saying that he could not print it, "in view of recent authoritative medical opinion." At that date the most authoritative medical opinion in the world had already confirmed the specific action of trypsin on cancer, but the opinion of the I. C. R. F. Committee and the Middlesex Hospital was alone known in this country.

It is an amazing index of the power of authority over the human mind, or, at any rate, the British mind, and of the totally unscientific attitude of public opinion, that it should be possible for an official body to publish, two years in succession, a condemnation of a remedy, without having any voice in the whole country except Dr.

Beard's and mine raised to ask for the evidence and further, that when the demand is made in the leading scientific journal, it should be possible simply to ignore it without a single person asking why, or even drawing attention to the fact. In order to recognize what the power of names and positions is, let us suppose that the Committee had announced a discovery, and that Dr. Beard, of whom the Director of the Research and his second in command are pupils, had published a denial of it, without a word as to the grounds for his opinion. No one would have paid the slightest attention to him, and rightly so. The distinction between the two cases is simply that in the actual one whatever the Committee chose to say was supported by the Prince of Wales and various eminent doctors, who, of course, were wholly dependent for their information upon what they were told to say. Thus a high-sounding name, royal support and an official position have enabled all the principles of scientific publication to be contemptuously flouted, and a public challenge to be ignored—no one saying a word. The whole thing sounds incredible, but the thing has happened. It was a most fortunate chance for, at any rate, a few patients that my *Daily Mail* articles appeared just before the I. C. R. F. report. Otherwise the editor, "in view of recent authoritative medical opinion," could scarcely have consented to their publication.

As for the medical press, the report was allowed to pass without any writer pointing out the remarkable contradiction between it and, say, the verdict of the German Cancer Research Institute, or the results of Dr. Zanoni, which have, of course, been noted in the American medical press, but have been ignored in this country.

It is not for a moment to be supposed that the sur-

geons and others who founded the Imperial Cancer Research Fund are responsible for the facts above recorded. Their enterprise was a wise and right and promising one, and the utmost honor is due to the surgeons, and especially to the most distinguished of their number, for their efforts to have the problems of cancer attacked afresh from the scientific side, the clinical attack having so appallingly failed. I only wish I were at liberty to mention the name of the world-famous surgeon and authority upon cancer to whom the Fund owes so much, and who, proving his open-mindedness, caused a letter to be sent to Dr. Beard, September 5, 1907, within a few days after the appearance of my article in the *Contemporary Review*, in which a request was made for directions as to the use of the ferments in a case which the writer and this surgeon "are anxious to treat exactly according to your method"—the method which, only a month or two before, had been publicly condemned by the Fund in the history of which this surgeon has played an indispensable part. Thus there are now two surgeons in Great Britain whom I should be honored to name here, and I deeply regret that I am not permitted to do so in the one case, and do not know the name in the other.

I need now deal only very briefly with the Middlesex Hospital Report (*Archives of the Middlesex Hospital*, vol. ix., Sixth Report from the Cancer Research Laboratories). This inquiry was undertaken at my demand in the *Pall Mall Gazette* last December. Dr. Beard's general directions were asked for and sent; but neither he nor I was consulted or informed in any way further. The inquiry was confided to two extremely youthful and inexperienced observers. The patients were obviously hopeless, if not moribund. Certain of the requirements

made by me in the *Pall Mall Gazette* were attended to, such as the testing of the injections and the avoidance of heating the syringe. When we come to examine the report we find the most astonishing omissions. The surgical history of none of the cases is given; there is absolutely no record of the urine in any case, not even as to the presence of albumin, much less the excretion of trypsin. There is not a word about the blood, so that we have no information as to leucocytosis or eosinophilia, still less the presence of trypsin in it. Thus we are entirely without evidence, which would have been quite easy to obtain, that trypsin ever entered the patients' blood. In these and all other points, from the qualifications of the observers onwards, we may contrast this inquiry with those in Berlin. Most of the patients received no adequate doses. The injections were so made that they caused great pain and discomfort ("this has always been the determining factor in causing the patient to plead for a discontinuance of the treatment"), and we are warned as to the "occasional production of inflammation or even suppuration." As the editorial writer of the *General Practitioner* has pointed out, this alone would entitle us to disregard the report, and, in the absence of any inquiry by modern clinical methods, we may probably agree with a correspondent of that journal who questions whether active trypsin ever entered the patients' blood. These brief comments may be concluded by the quotation of an early paragraph: "Two cases of carcinoma were placed on trypsin treatment in May, 1906, in the cancerwards of the Middlesex Hospital, but with negative result, there being no improvement in the patients, nor was the progress of the growth influenced by the trypsin injections." On turning over the page the reader will

find, to his amazement, that the second of these patients had *only one injection*, and that of a 2 per cent. solution so called. If this fact does not serve to indicate the observers' bias, nothing will. A few favorable results were observed, such as diminution of pain in one case, the disappearance of obstruction in the rectum in another, a stationary condition in a third, and certain microscopic features in two others; but the observers attach no importance to them, nor do I, though they may possibly indicate that the local disasters which followed the injections may not have involved the entire destruction of the ferments. One case underwent enormous loss of weight "during the special treatment, whereas he had remained in a fairly stationary condition previous to the commencement" of it. This alone would suffice to indicate the fashion in which the treatment was carried out.

The observers conclude, and the conclusion is concurred in by the distinguished surgeon who was in charge of the patients, as by the director of the laboratories, that "the course of cancer, considered both as a disease and as a morbid process, is unaltered by the administration of trypsin and amylopsin."

Such is the scientific and clinical quality of the report which was hailed with joy as conclusive by the *British Medical Journal* and elsewhere, while the diametrically opposite result already published by Prof. Von Leyden and Dr. Bergell was absolutely ignored. I specially regret that we have no information as to the urine. Obvious considerations would have prevented me from making this demand along with the others in the *Pall Mall Gazette*, even had it occurred to me for a moment that this most elementary of all observations would have been ignored.

CHAPTER XXI

CONCLUSION

“WHERESOEVER the carcass is, there will the eagles be gathered together,” and wheresoever cancer is, there will liars and thieves be gathered together, unless they are driven off. Less merciful than the birds of prey, these beasts of prey do not wait until life has fled, but prey upon the living. Not once but many times I have used such opportunities as have been mine to warn the public against the cruel and murderous blackguards, with their nostrums and lies, who prey upon those whom cancer has already marked down for them. Such are the facts of experience that any one who proclaims a remedy for cancer is suspect of being a quack. In this very instance it is the case that practically all the “help” I have received during the past eighteen months has been the worthless and self-interested “help” of a few quacks, nearly all of them qualified quacks—in whom every organized profession on earth abounds—who have raised their voices to swell their pockets. It is necessary, then, briefly to observe that Dr. Beard is not a medical man but an embryologist, and that I do not practice medicine. Dr. Beard may not care that I should speak of his tireless labors, his enormous correspondence, his prompt and exhaustive advice, refused to none, and all this and much more for love alone. I will insert against his wishes the fact that he has gladly defrayed the cost of treating poor

patients by his method. As for myself, though I have seen many patients and watched them from day to day, I have taken nothing from any one—on the contrary. My own line of work has been gravely interrupted, with serious effects of more than one kind; and if the reader were fully acquainted with the details of my days since January, 1906, he would understand how it is that I permit myself to express with simple candor my opinion of the writings of medical journalists and others who have never seen a trypsin injection in their lives, and know no more of the subject than I do of Sanscrit; persons who have made no sacrifices of any kind, whether of time, or thought, or money, have run no risks of the loss of personal reputation, but have not hesitated, in their brave anonymity, to demand apologies, to suppress facts, to misquote, to make every conceivable misrepresentation, and in effect to deprive tens of thousands of cancer-patients, already beyond all hope of surgery or other means, of the practical certainty of relief from pain and fœtor, and the promise of much more, which the new treatment would have afforded them. It matters little to me now that this anonymous and motley crowd should have made personal attacks upon myself: it certainly matters nothing to Dr. Beard that they should have spilt their venom on him: "there are some praises which reproach, and some reproaches which praise," as La Rochefoucauld said: but it does matter that any opposition to a useful remedy for cancer should have been successful even for a day, or even in one single case—let alone for nearly two years and in tens of thousands of cases. There is blood upon many hands.

I foresee that some critics, partly out of malice and partly in self-defense, will accuse me of having been "pre-

mature" in my writings. But how otherwise could the subject have passed the stage at which discussion was "premature"? The customary channels were closed. There was, indeed, much premature writing and speaking on the subject. Perhaps the Director of the Imperial Cancer Research Fund was premature in stating at Montreal, in July, 1906, that trypsin had been tested and was worthless—a curious way of stating the fact that if he had tested his trypsin he would have found it worthless. The truth is that, as human nature is constituted, the new thing always appears premature to the majority; this really means, not that it is premature, but that they are immature. If the profession and the public had known a few elementary facts about ferments two years ago my writings would not have been premature simply because my readers would have been prepared for them. I was blamed because they were ignorant; as I was until I looked into the matter. But there was no possible means of removing the ignorance except by drawing attention to the subject.

I hope that this case has a real sociological meaning. I hope it means that the press will furnish the true and efficient means of protection against the increasing officialism of all activities, including even scientific thought, in our day. Officialism there must be, and Research Committees and so forth: but not until I hear that Shakespeare was a syndicate, that gravitation was discovered by a committee, that *Tristan und Isolde*, which was created, music and verse, by one mind, is inferior to the latest musical comedy, whose composers and authors would sink a barge well lost—in short, not until I cease to be convinced that nothing but personality ever did anything worth doing, shall I cease to protest.

that, however splendid our apparatus for research, or our schools of art, or our established creeds, there will arise some day a man, within or without the official barriers, and will flick them away like a crumb from a cloth. If the race ceases to produce the original man, its progress will cease. We need not be deluded: half a dozen dwarfs may outweigh one giant, but the analogy of mass has no application in the spiritual world. The united labors of all men now living could not write another *Tristan*: and though from one mediocrity you may obtain, by a rare inspiration, something good, from a committee of mediocrities you will certainly never obtain anything but a mediocre result; if one of them does have an inspired moment, the rest will see that no harm comes of it. We foolishly repeat that two heads are better than one: but it depends on the heads. How many Donizettis would it take to write one *Choral Symphony*? Not only does one wise man's verdict outweigh all the fools', as Browning said; but in two seconds he may add more to the eternal wealth of mankind than they in all their lives, be they never so endowed with money, and opportunity, and authority. The world is governed, said Goethe, by wisdom, by authority, and by show. When a great medical journal propounds ignorant and inexcusable misrepresentations of a new truth which has not come through the only mechanism that excuses a truth for being new, or when a great research institute pronounces without any knowledge upon the work of some one whose claim to be heard is merely the idle one that he is a sincere and assiduous lover of truth—then the world is governed by authority and by show. It is time that, in these days of organized research and social mechanism in general, we should remind ourselves of the known facts of the genesis

of all discovery and all new creation, whether in science, or art, or any other sphere. I have lately¹ discussed this subject, but I cannot neglect the opportunity of pointing the moral here.

Let us take a lesson to ourselves. "History warns us," says Huxley, "that it is the customary fate of new truths to begin as heresies and to end as superstitions." This is one of that small band of epigrams which are at once profound and true. Now the doctrine that there is no remedy for cancer but the knife was at one time a heresy, and arose when the science of diagnosis had so advanced that curable maladies, formerly thought to be cancerous, were properly identified. This new truth was until lately true; but it had the "customary fate," and ended, or is ending, as a maleficent superstition. The newer truth that certain ferments are remedial in cancer began as a heresy, in opposition to the orthodox view that the knife alone is a remedy for cancer. This new truth will shortly begin to take its place as an orthodox dogma. But let us beware. At any moment in the immediate or the remoter future, when the value of the pancreatic or other known ferments is a commonplace, when, perhaps, men and institutions exist to demonstrate it, or great chemical laboratories to prepare, or even manufacture, these ferments—in a word, when vested interests are involved, as the Church is involved in its dogmas, or the proprietor of anything in our conventional beliefs regarding property—there may arise a new heresy. Some one may discover a new ferment which does in hours what trypsin does in weeks or months, *some one may discover how to prevent the occurrence of cancer*—and

¹In two lectures on "Biology and Progress," delivered at the Royal Institution, March, 1907.

how shall we behave? If we are not to learn from the past—and each generation makes this same mistake, in art, and science, and religion, and politics, and everything else, while deriding its predecessors for the very same act—we shall lie and malign, and suppress, and misrepresent, and obstruct, and deny. As the first disciple of Dr. Beard, I myself, if I live to see such a day, as I very probably shall—I myself will be the foremost to declare that nothing can possibly be better than trypsin and amylopsin, or half so good; that the innovators are irresponsible, and ignorant, and dishonest; that the established truths which have done such service are in danger at the hands of those to whom all truth is an offense, that the heretic has no official status, has not received the license of the "Trypsin Institute," let us say, and that, as will likely enough be true, he is "not even a medical man." Only do I hope that if and when this event happens, some one will quote these present words and put me abruptly to silence.

So much for this great sociological issue, and now for another, which is psychological and of no less importance in the progress of knowledge. It is commonly asserted that the foundation and root of all science is skepticism, the spirit which questions and will not believe until it must: I have often discussed the importance of this attitude. The performance of this function is the chief and only use of what we may call the inferior class of scientific minds. These play the part of heredity as opposed to variation in the realm of organic evolution, and of conservatism as opposed to liberalism in the State. But it would be a ludicrous denial of the major facts in the history of knowledge to suppose that the opposite state of mind, that of faith, has no place therein. It would be

easy to demonstrate, but surely superfluous, that the great achievements in science have one and all been made by men who believed in some idea before the acquirement of conclusive evidence in its favor. It was this faith which inspired them to seek and reveal the evidence which ultimately established their case: and only by such faith can the mountains of prejudice be moved. The sober onlooker talks of infatuation or monomania, and duly performs the skeptical function, which is so easy and so safe. All great enterprises appear insane to the onlooker at first. But the believer goes on and on, turning neither to the right hand nor to the left. Often enough he is wrong, whereupon the skeptics, who are always in the majority, congratulate each other upon their superior acumen. But sometimes he is right: and then, and then only, and never otherwise, science moves on.

Consider the case in point. A host of practitioners, disbelieving, have tried the new remedies and obtained nothing but failure. The disbeliever, since he disbelieves, attributes his failure to the nature of the case: and the matter is closed for him. But the believer, since he believes, attributes his failure to himself. According to his faith, such and such a result should have been obtained. Since it was not obtained, it is plain that *he* has gone wrong somewhere. He looks for sources of error—such as the use of inert injections—removes them, and, if his faith is well-founded, he succeeds. Observe the function of the psychological state called faith in this respect. How innumerable are the instances which might be adduced. A Newton conceives a law of universal gravitation, and, since he is a Newton, this law inspires him with faith in its truth. He has practically no evi-

dence: just as Dr. Beard had absolutely no experimental evidence whatever when he announced that trypsin must be remedial in cancer. He sets to work to make the necessary calculations from the *data* of a Kepler, in order to prove the truth of his theory—which, like all theories and truths in the first instance, is his own peculiar and unshared possession. The calculations are made and do not tally with the theory. Any one else, having made them and found them discrepant, would contentedly drop the whole matter. But the Newton, since he has faith, returns to his laborious task, finds an accidental error in reckoning, and produces a new series of calculations which prove his faith to be founded on the rock of fact—and all future ages are enriched with a new truth, the only kind of wealth which neither moth nor rust can corrupt, and which can be used and spent and remain inexhaustible, the treasury of true ideas being the fact of which the inexhaustible purse of Fortunatus was a symbol. Now it is right to doubt when evidence is inadequate, or rather, it is right for all men but one to doubt: but it is also well that one man, he who conceived the new thing, should believe, evidence or no evidence. Let the others boast their “scientific caution,” which is more often than not only cowardice, or ignorance, or lack of imagination, or desire to be left alone, the analogue of inertia in the physical world: but when there fails a supply of men who see, though only in a vision, a goal which to all others is a delusion, and who press towards it though all others declare that to leave the beaten track is to land in shallows and miseries—then all progress in all spiritual spheres, art or religion or science, will cease, and the sooner the sun grows cold the better—unless, as Professor Lowell declares against the critics who have

not his opportunities, there be intelligent life upon Mars.

Let me endeavor to make good a further point with the aid of the mighty German I have just quoted. Goethe somewhere says, "*We learn to know nothing but what we love*; and the deeper we mean to penetrate into any matter with insight, the stronger and more vital must our love and passion be." This is one of the most profound and universally significant of psychological truths, and has yet to be recognized by those who commonly write as if knowledge and intellectual activity were entirely unrelated to the emotional nature. The common view survives from the disproved "faculty" psychology. But all the history of the deeds of mind proves the truth of Goethe's words. When the conception of universal gravitation came to Newton, he was not thinking how to earn the absurd knighthood of his later years, nor of how many guineas per thousand words he could obtain for writing on the subject, nor how to score a point against a colleague. He was deeply in love with the subject, and his love led him to the truth. It is so with the creation of every great work of art. The writer who asks "Will it sell?" as he writes, will never write anything fit to sell: the dramatist who asks "Will it draw?" will never write a play fit to draw any but moths and their like. Nothing supremely great, nothing too hard for the teeth of time, was ever achieved except for the love of it. The universal goddess who is the mother of all past achievement and whose fertility is not yet exhausted, being inexhaustible, has but one question which she asks of all who woo her—poet, painter, pathologist, and all others. "Do you love me for myself alone?" she asks. The maiden asks the same wise question, but she may be

deceived. Nature, however, is not mocked. The wooer who is after her money, or position, or the chance of spiting some one else, cannot cozen her, protest he never so loudly that his heart is hers alone. But she will admit to her embraces all who do indeed love her; and never to such will the joy of fatherhood be denied. The fruit of their love may be a lyric or an epic, a single fact of observation or a universal truth, but fruit, and sound fruit, there will always be. The stronger and more vital the lover's passion the worthier will be its product.

Such, in image, is the parental history of all the children of men's minds and souls: and we must beware lest we forget it. "We learn to know nothing but what we love": and without lovers of knowledge or beauty for their own sake, nothing worthy, nothing viable, will ever come to birth, though the whole earth were covered with one huge laboratory or one huge school of art.

We all agree that it is the emotional nature which makes the artist. Music is not mere applied mathematical acoustics, nor poetry applied philology. The composer or the poet, the artist of any order, must have the soul of an artist, a heart that beats in time with the music of the spheres and the tones of human life. We usually suppose, however, that in science and philosophy the emotional requirement is *nil*, that intellect is everything, and that, indeed, any kind of emotion is a hindrance and a defect. This common doctrine wholly ignores the psychology of knowledge, as Goethe has indicated it for us. Only the man who is driven by the motor-power of disinterested interest, or love, only the man who lives for love of his subject, and who would find life worthless without this love—only he will reach the goal.

Science now offers a career to thousands, where for-

merly it was followed only by the inwardly directed or predestined few. But we must be warned in time. Nature will have no father for her spiritual children but those who love her for herself alone, and she cannot be deceived. Study the biographies of the "kings of thought," "the splendors of the firmament of time," as Shelley calls them, and see how broadly it is written that each of them might truly have described himself to nature as "One born to love you, sweet!" To such a one his love is his "whole existence": it is not immune from error, but it is never sterile. Only of such disinterested and whole-hearted love is knowledge born, the knowledge so born has brought mankind thus far, and, unless the supply of true lovers fails, or men imprison or emasculate them, future knowledge so born will yet transmute the conditions of life and even human nature itself, not without the pains and groans of travail, which shall burst into sphere music before the earth's race be run.

The sun is always rising somewhere upon the sphere of the mind; there are men who love the past, the sunset; men who glory in the sure and strong thing, the sun at noon; but the prayer for him who believes that the best is yet to be, and who would rather hail a false dawn for a time than deny a true one, is this: *Let neither old age, nor habit, nor love of self or ease, nor any other thing, be permitted to obscure the eastward windows of my soul.*



