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The most important
medical news of our time
LAETRILE
(THE ANTI-CANCER DRUG)

**CONTROL
FOR
CANCER**

The authorized story
by **GLENN D. KITTLER**

Comments and evaluations from
world-famous research scientists and
practicing physicians, with documented
case histories from hospital records

**"TO MY MIND, TRAINING, AND EXPERIENCE,
[LAETRILE] IS THE IDEAL DRUG
FOR THE TREATMENT OF CANCER . . ."**

*—Dr. Manuel D. Navarro, Associate Professor of
Medicine, University of Santo Tomas*

**"LAETRILE IS A POWERFUL
TOOL AGAINST CANCER"**

*—Dr. N. R. Bouziane, Professor of Pathology and
Biochemistry at the University of Montreal; Dean
of the American College of Bio-Analysts; Director
of Research Laboratories and Chemotherapy Spe-
cialist of the Tumor Board at the Hôpital Ste.
Jeanne D'Arc*

LAETRILE: CONTROL FOR CANCER

tells the complete story of the greatest medical discovery of our time—an effective anti-cancer drug. Here are the men who made the breakthrough possible: Dr. John Beard who made the revolutionary discovery regarding the nature of cancer; Dr. Ernst T. Krebs and his son, Ernst T. Krebs, Jr., who devoted their lives to the development of the drug Laetrile, which controls cancer in much the same way that insulin controls diabetes; and the many other dedicated physicians and scientists whose struggles have helped to bring Laetrile out of the test tube and into the hospitals and doctors' offices.

Here is the story of Laetrile itself and how it works, destroying cancer cells without harm to other tissues; actual case histories, medical records, reports and evaluations from scientists and from doctors who have treated patients with Laetrile.

LAETRILE: CONTROL FOR CANCER is required reading for every family, every cancer research scientist, every physician.

Glenn D. Kittler, author of LAETRILE: CONTROL FOR CANCER and a well known journalist, has written widely on scientific subjects. His work has appeared in *Reader's Digest*, *The Saturday Evening Post*, *The American Weekly*, *Catholic Digest*, *Sign*, *Pageant*, in numerous other national magazines and in anthologies. He has been a newspaper reporter in Chicago and Norfolk and an editor of *Coronet*. Mr. Kittler's fourteen books include *Triumph*, *The Papal Princes*, and *Equatorial Africa: New World of Tomorrow*.

LAETRILE
(THE ANTI-CANCER DRUG)

**CONTROL
FOR
CANCER**

by Glenn D. Kittler

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**CONTROL
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CANCER**

**To Dr. Arthur T. Harris
Friend and Fellow-Beardian
In Memoriam**



ACKNOWLEDGMENTS

This book is the result of ten years of work. The work has not ended, any more than the story the book tells has ended. The story will end when the fear of cancer has ended. This book tells how that end can come about. These ten years have made me more than a reporter of the Laetrile story. I have become a personal friend of the men who have lived the story; inescapably, I have become intimately involved in their trials, their failures and their successes, and in doing so I feel I have become their co-worker. In journalism, it is said that the two great stories still to be written are the conquest of cancer and the Second Coming of Christ. I have been rarely privileged in getting the first story; I dare not hope for the luck to get the second.

I am most grateful to the men who gave me the benefit of their time, knowledge, experience and friendship, upon all of which this book is based. I am grateful, first of all, to Dr. Ernst T. Krebs, Sr., and Ernst T. Krebs, Jr., who developed Laetrile and without whom there would be no story at all. I am grateful to Andrew R. L. McNaughton, of Montreal, Canada, and his staff of The McNaughton Foundation, who guided Laetrile over the hurdles to the tests which provided the present confidence in the drug. Dr. N. R. Bouziane, of the University of Montreal, Dr. Manuel D. Navarro, of the University of Santo Tomas, and Dr. Ettore Guidetti, of the University of Turin, were important guides in my own understanding of the Laetrile science, both personally and in correspondence. Dr. John

A. Morrone, of the Jersey City Medical Center, was especially invaluable in this area in the preparation of manuscripts. The wisdom, patience and insight which Edward H. Spicer, president of Spicer-Gerhart, the pharmaceutical company, brought to the Laetrile work made him a father to us all. Also, it was due to his respected position in science that the foreign work with Laetrile continued when the American work could not. In 1952, I was introduced to the Laetrile work, and consequently to all the aforementioned, by the late Dr. Arthur T. Harris, of California and the Union of South Africa. All Beardians regret that he is not here to share in these final triumphant hours—but, then, sometimes we are not too sure that he isn't.

I also wish to acknowledge the Cavalero Foundation of New York City for its interest. Charles H. D. Robbins, of The American Weekly, suffered through the editorial headaches and heartaches of the project with me for the full ten years. Hy Steirman, of Paperback Library, Inc., friend, my co-author of other works and the publisher of this book, came to the rescue time and again with encouragement, enthusiasm and support. And the only person who really knows what these ten years have been is Evelyn Singer Haber, my agent. She knows, too, that they have been worth it.

G.D.K.

FOREWORD

In **LAETRILE: CONTROL FOR CANCER**, Glenn Kittler has produced an outstanding piece of factual reporting. He has at the same time managed to treat a most difficult subject with understanding and restraint. All of us connected with the Laetrile program are deeply indebted to him.

At the present time, as is well known, surgery and radiation are the commonly accepted methods of dealing with cancer. Although chemotherapy (use of chemical compounds) is now considered respectable, its potential is just beginning to be appreciated by doctors and researchers outside the abstruse and relatively new field of biochemistry. The acceptance of chemotherapy, as of equal and often superior value to surgery and radiation, has been further retarded by the extreme toxicity and other unfortunate side effects of most existing chemotherapeutic agents.

In **LAETRILE: CONTROL FOR CANCER**, Mr. Kittler tells the story of a promising chemotherapeutic agent being used, thus far, experimentally in the treatment of terminal cancers. With this drug, Laetrile, it has been demonstrated that there are no toxic or other adverse side effects.

Furthermore, the evidence accumulated by our medical advisers convinces us that if Laetrile is used in early cancers there need not be terminal cases. And when proper diagnosis is available to identify cancer in its pre-tumor, pre-clinical stages, we can confidently expect that

Laetrile will remove even the dread of early cancers from our lives.

These are broad claims to make about a cancer drug. Likely they will provoke considerable discussion and possibly even some controversy. Honest controversy leading to a thorough examination, with the public watching, can be a healthy and constructive thing. Such is the real purpose of this book.

Laetrile is a complex chemical compound developed from a very basic explanation or theory as to the cause of cancer. This is the *Unitarian or Trophoblastic Thesis of Cancer*, which holds that the placental trophoblast cell and the cancer cell are one and the same thing.* The theory was founded on the research of Dr. John Beard (1858-1924), of the University of Edinburgh, in Scotland. It is a very persuasive theory and one which has, over the years, provided a logical explanation for each new fact about cancer as it was discovered.

The view currently held by the majority of cancer researchers is that there is a multitude of different kinds of cancer. The Beardians, on the other hand, hold that there can be but one basic kind of cancer. They maintain that the constant malignant component of all manifestations of cancer is the trophoblast cell. It is their thesis that all tumors, both malignant and benign, are composed of varying proportions of trophoblast cells and normal somatic cells. A fully benign tumor, therefore, would be one in which the trophoblast component is zero.

In choosing between these two mutually exclusive explanations, let us remember one simple criterion which applies equally in all fields of scientific research. This is: "The value of a theory resides primarily in its usefulness."

A useful theory is one which brings order to the confusion and chaos of facts which formerly appeared to be

* See chapter 5.

unrelated. A useful theory should provide a logical explanation, without contradictions, for all of the observed facts. Further, one should be able to predict from such a theory facts previously unknown and to verify these facts by subsequent observation.

The Unitarian or Trophoblastic Thesis of Cancer, on which the formulation and action of Laetrile is based, is the only theory which meets both of these requirements. It provides a logical explanation for all of the currently known facts of cancer; it has enabled previously unknown facts to be predicted and later verified in nature.

Laetrile is an anti-cancer chemical whose development is implicit in the *Trophoblast Thesis of Cancer*. From this thesis, the rationale of the drug follows naturally.

The important question now should be: Does Laetrile work as predicted? Surely the answer to this question is a matter of honest, unbiased clinical trial and observation.

Over the past years, quite extensive data has been accumulated by highly competent clinicians in various parts of the world on the use of Laetrile in hundreds of cases of terminal cancers. Terminal cases are those so far advanced that surgery and radiation are conceded to offer no further hope. The correct interpretation of the results obtained by Laetrile therapy in such terminal cases is often made difficult by the previous surgery and radiation. Even so, it should now be abundantly clear to any open-minded observer that in these terminal cases significant results have been obtained with the Laetrides which cannot be fully explained as spontaneous remissions, as due to psychological factors or as the delayed effects of the previous radiation or surgery.

Interesting as it may be to debate, on theoretical grounds, the relevance of the Trophoblastic Thesis and the Laetrides in the treatment of cancers, let us not at the same time ignore the world of reality. Hundreds of millions of dollars are spent each year on cancer research.

Notwithstanding this research, the incidence of cancer is still increasing. According to The American Cancer Society, one out of four of us now alive will develop cancer, one out of six of us will die of it.

Let us devote a minute fraction of the time, money and energy, now being expended on largely unproductive research, to the development and evaluation of the Laetrile. Let the controversy between chemotherapy, surgery and radiation, brought into the light of day by this book, result in constructive action. Let the development of the sensitive diagnostic test for cancer, now under way, be speeded. Let clinical trials of Laetrile at all stages of cancer be initiated. Let these tests be carried out in close and friendly cooperation with those who understand the theory on which Laetrile is based, otherwise the results of these tests may be misunderstood and easily misinterpreted.

With the positive cooperation of The American Cancer Society and the American Medical Association, cancer could soon join the list of those diseases which mankind no longer fears. The rewards in terms of human happiness alone could be immense.

Andrew R. L. McNaughton

The McNaughton Foundation
2015 Drummond Street
Montreal, Canada

CHAPTER 1

The most important medical news the world can hope to hear is that the mystery of cancer has been solved. It is in the mystery that the fear of cancer has its roots. So dreaded is the disease that few of its victims are told by their doctors and families that they have it. Even heart diseases, which alone take more lives than cancer, are not as feared. A man with a heart condition can be put on a strict regimen which can give him an almost normal life free of fear. But cancer is different. The educational program of The American Cancer Society has done much to send people to their doctors at the first signs of suspicious changes in their health and has certainly accounted for the detection of countless early cancers which apparently responded to conventional therapy. Yet even in these cases the fear lingers on because the mystery remains, and there is always the haunting torment that the disease will recur. In most cases, it does.

The news, then, that the mystery has been solved puts an end to the great fear, and this in itself is a vital contribution to the universal peace of mind. According to a number of international research scientists, the mystery has indeed been solved. Moreover, based on the clues to the mystery, these scientists have produced a drug, called Laetrile, which they believe offers the best hope in the treatment of the disease. Their conviction is the result of hundreds of tests on terminal cases in a dozen countries. Positive reactions in these advanced cases have led to the opinion that, used early enough, Laetrile can prevent

fatal cancers. Furthermore, when an accurate diagnostic test is developed that will make possible the identification of cancer in its pre-tumor, pre-clinical stage, Laetrile will, it is believed, prevent the appearance of early cancers now usually requiring treatment by surgery and radiation.

All this, to be sure, sounds like extreme optimism, but there are scientific grounds for it. There is no mystery about the Laetrile science, no secret formulas, no guess work. Laetrile proponents contend:

1. The cancer cell is a normal body cell which plays a vital role in the reproduction of life but which, as cancer, appears abnormally at the wrong time and in the wrong place.

2. Under normal conditions, the cell is kept under control by the pancreatic enzymes.

3. Even when the cell appears abnormally, it can be destroyed by the enzymes from the pancreas.

4. When the enzymes fail to appear in adequate quantities, the cell proliferates and demonstrates itself as cancer.

5. Cancer is, therefore, like pellagra, scurvy and diabetes, a deficiency condition which, like these diseases, is responsive to medication.

6. Cancer elicits specific biochemical circumstances which allow Laetrile to be broken down at the site of the growth and perform its action of killing cancer cells.

Research supporting these contentions has been done by researchers and physicians affiliated with major universities, such as the University of Montreal, Canada; Louvain University, Belgium; the University of Santo Tomas, the Philippines; and the University of Turin, Italy. Work has also been done by prominent scientists in

England, Japan, Mexico, the Union of South Africa and the United States. Many of these men have reported their observations in leading medical journals. Some of their comments:

—Dr. Manuel D. Navarro, Associate Professor of Medicine, University of Santo Tomas:

"In Laetrile we truly have an ideal anti-cancer drug."

—Dr. N. R. Bouziane, Professor of Pathology and Biochemistry at the University of Montreal, Dean of the American College of Bio-analysts, Director of Research Laboratories and Chemotherapy Specialist of the Tumor Board at the Hôpital Ste. Jeanne-d'Arc:

"In our investigation, some terminal cases were so hopeless that they did not even receive what we consider the basic does of 30 grams. Most of the cases, however, became ambulatory and some have in this short time resumed their normal activities on a maintenance dosage."

—Dr. Shigeaki Sakai, Dr. M.Sc., internist, Matsuyama, Japan:

"Administered to cancer patients, Laetrile has proved to be quite free from any harmful side-effects, and I would say that no anti-cancer drug could make a cancerous patient improve faster than Laetrile. It goes without saying that Laetrile controls cancer and is quite effective wherever it is located."

—Dr. John A. Morrone, attending surgeon, Jersey City Medical Center, Jersey City, N. J.:

"The use of Laetrile intravenously in 10 cases of inoperable cancer, all with metastases, provided a dramatic relief from pain, discontinuance of narcotics, control of fetor, improved appetite and reduction of adenopathy. The results suggest regression of the malignant lesion."

Despite these encouraging reports, the Laetrile work still progresses slowly and with caution. This is both wise and essential. No other disease so stirs the emotions of those touched by it; no other disease has been the sub-

ject of such heated scientific controversy. Any premature deductions would, therefore, spark a cancer panic and send scientists off into voluble defense of their pet theories. To prevent both, the Laetrile proponents have worked quietly, steadily accumulating scientific evidence that can speak for itself.

Spearheading the work for over thirty years has been the San Francisco father-and-son team of Dr. Ernst T. Krebs, Sr., and Ernst T. Krebs, Jr. Dr. Krebs has given most of his adult life to the work; the younger Krebs has given all of his. Together they developed the Laetrile formula. To Ernst Krebs, Jr., fell the chore of confirming the science on which the formula is based. In doing so, he crisscrossed the hemisphere, tracking down clues to the nature of cancer in a score of medical libraries and laboratories. His research required him to teach himself German, French and Spanish and to acquire a working knowledge of thirty-two different branches of medical science.

The concept of cancer and of cancer therapy which the Krebses were eventually able to present to the science world was revolutionary, and as such it was suspect. To be able to grasp it required as much knowledge as had gone into it, and in this age of specialization there is a dearth of men with sufficiently broad scientific backgrounds. Also, in 1953, just as the Laetrile work was making headway, it was evaluated by the California Cancer Commission and its efficacy was questioned. Abroad, however, the research continued, although on a limited scale. It seemed as though the challenge which Laetrile needed—numerous tests to determine a pattern of effects—would never be presented.

Then, late in 1958, Laetrile came to the attention of The McNaughton Foundation, of Canada, sponsors of independent research, and it was through the Foundation's efforts that Laetrile was given an extensive appraisal

in Canadian hospitals. As a result, a growing number of Canadian doctors lost any doubts they might have had about Laetrile because of its California experience. Actually, the tests were not easy to arrange, and in explaining why the Foundation went to great lengths to do so, its president, Andrew R. L. McNaughton, said:

"Individuals, even well-qualified scientists, who advance ideas contrary to those accepted by ruling scientific opinion frequently encounter considerable difficulty in obtaining both financial support and technical facilities to enable them to carry out the investigations necessary to prove or disprove their controversial concepts. We feel, without in any way discounting the value of the emphasis currently placed on team research, that most revolutionary breakthroughs in human knowledge originate in the mind of an individual. We feel that there is a great unfulfilled need for an organization such as ours to provide the spiritual and physical environment which certain unorthodox investigators so badly require and find so difficult to obtain despite their qualifications."

In fulfilling the needs of the Krebses, the Foundation may well have fulfilled a need of the world: the eradication of fatal cancers.



CHAPTER 2

The body cells which can develop into cancer cells exist in every human being. The parts these cells play in the reproduction of life and in cancer are explained in Chapter 5. In the reproduction of life, they are both normal and essential cells. It is when these cells exhibit themselves as cancer that they can be described as behaving abnormally. But even when they behave abnormally, Nature is prepared for them. It is a scientific fact that Nature has equipped the human body with all the defenses it needs against diseases: it is when the defenses break down that the disease flourishes. Even when this happens, Nature is prepared, in providing drugs which can be found in plants, minerals and the organs of other animals. The task of identifying these drugs and developing them for use in human beings is the dramatic crusade of scientists.

Another defense which Nature provides are the symptoms of a disease—the aches and pains and body changes which indicate that something has gone wrong. Doctors use these symptoms to diagnose a disease, and the earlier diagnosis can be made the better chance there is for quick and effective therapy. The American Cancer Society has widely publicized seven danger signals of cancer,* and yet is it true that when these symptoms become ap-

* (1) Any sore that does not heal; (2) a lump or thickening in the breast or elsewhere; (3) unusual bleeding or discharge; (4) any change in a wart or mole; (5) persistent indigestion or difficulty in swallowing; (6) persistent hoarseness or cough; (7) any change in normal bowel habits.

parent the cancer may be already well advanced. Also, it is the nature of people to disregard danger signals which don't seem very dangerous at first, and by the time most of them finally go to their doctors they are in serious trouble. The American Cancer Society wisely advocates regular check-ups in order to detect early cancers, but a common regret among doctors is: "How often do we see early cancers?"

When early cancers are detected, they are usually treated with what are regarded as the tried-and-true therapies of surgery and radiation. But surgery and radiation do not affect cancer itself: they are merely treatments for another symptom of the disease: the cancer growth or the cancer damage. They do nothing to change the circumstances which started the cancer off in the first place; they can do nothing to prevent the circumstances from arising again; they are sometimes detrimental because of the extent to which they must go to appear effective; and the day inevitably comes when the surgeon simply cannot cut any more out of his patient and the radiologist simply cannot burn any more into the patient. This futility is one of the many heartaches of the medical profession.

And the heartache will persist until the fact is faced that Nature has provided a way to control cancer similar to her own: through chemistry.

Numerous attempts have been made to attack cancer through chemistry, such as with nitrogen mustard gas, and the medical complaint against such efforts is that they have harmful—sometimes serious—side effects. If so, then a simple fact should become immediately clear: the chemistry of the particular drug is wrong. When the chemistry is right—when it is based on Nature's chemistry—then it should work. And it should work safely.

In the dozen years that Laetrile has been used on hundreds of patients around the world—involving thou-

sands of injections—there has not been a single report of a harmful side effect. There can be only one explanation for this: Laetrile's chemistry is correct.

But does Laetrile do its job?

Medical ethics require that experimental drugs be restricted to terminal cases—patients for whom surgery and radiation can do no more. From experience, doctors can rather accurately predict how long a terminal patient will live. When a patient on such a time-limit is then given an experimental drug and lives beyond the predicted period, surviving not only for a few days or a few weeks but for a few months, even a few years, then it is obvious that something has happened. And when the patient appears to have recovered his health, there can be no doubt that something has happened. However, such cases are frequently said to have undergone a spontaneous regression (decrease of the cancerous action for unknown reasons) or to have experienced belated benefits from the surgery and/or radiation. But when the pattern of improvement in patients receiving the drug is consistent, it becomes unscientific and illogical to attribute the improvements to the happy accidents of mystery or delayed action.

Doctors using Laetrile have taken these accidents into consideration in evaluating their cases and they have come to the conclusion that the improvements occurred because of the Laetrile.

One case in point was a 44-year-old Canadian radio announcer who, in May, 1960, reported to his doctor that he had a persistent sore throat with increasing difficulty in swallowing. On seeing the condition of the man's throat, the doctor ordered a biopsy (microscopic examination of a small specimen of the tissue) and the condition was identified as cancer. The doctor recommended surgery. But the patient, knowing that surgery might affect his voice and therefore his livelihood as an

announcer, refused it and asked for treatment by radiation.

He was examined by Dr. Jacques Daneau, chief radiologist at the Canadian Radium Institute, a government institution and one of the best of its kind, who reported:

"There is no doubt that these lesions are most unyielding and radio-therapy is practically of no use. This kind of lesion is radio-resistant and the results of the radiation are generally not encouraging."

Still the announcer refused surgery, and for the next three months he underwent cobalt therapy. In August, doctors saw that the growth was spreading and they urged immediate surgery, but again the man said no. He was not seen again until March, 1961, when he was brought back to the hospital. For six months he had been unable to take solid foods. Examination showed that surgery was now impossible. It was too late. The case was now terminal.

But now Laetrile could be used. The announcer received his first Laetrile injection on March 22. On April 4, this statement was added to his case history:

"As the patient was leaving the hospital there was an unbelievable change. General health is progressing at the same time as the lesion is diminished and replaced in the perifocal area by new protective epithelium."

In other words, the cancer was receding and was being replaced by normal cells. The man continued to receive Laetrile. On June 27, this:

"The patient has gained eleven pounds. The lesion has almost disappeared."

On July 25:

"Patient is feeling well and for the first time in many months was able to eat a steak. Same treatment is being carried on."

The treatment then was two one-gram injections a week, but as the man continued to improve the injections

were decreased to one gram weekly, and in December the doctors reported:

"After a complete clinical check up of this patient we have found him in excellent condition and have decided to stop the Laetrile treatment for three months."

An important consequence occurred. The doctors observed that when the announcer went without Laetrile he experienced slight difficulty in swallowing and some voice change in the sixth week, but when the one-gram weekly injections were resumed these symptoms quickly disappeared. What was happening? This: The body chemistry which normally keeps cancer under control was not functioning properly in this man. Thus if there was one live cancer cell left in his body when Laetrile was discontinued it would multiply—again and again—just as it would multiply regardless of what kind of therapy he had received. With Laetrile, all that is necessary to keep the lingering threat of recurrence under control is maintenance injections. Throughout 1962, periodic examinations were made of the announcer as he remained on a maintenance dosage, and remained clinically free of the disease and was able to return to a normal life. There is no question, therefore, that Laetrile has done its job in this case.

Similar is the case of a Canadian woman who, at 61, had a breast removed in November, 1959. Biopsy established cancer with metastases (growths in other areas). For four months she underwent radium treatments in an effort to bring the metastases under control. A year later, in May, 1961, she was brought back to the hospital; she was very weak and completely unable to walk, she had difficulty in breathing and coughed severely. X-Rays showed involvement of the lungs to the extent that the case was considered inoperable. Laetrile therapy was begun, and the doctor reported:

"After a month we observed complete improvement.

The coughing has disappeared; she has no more dyspnoea (breathing difficulty). Clinically the patient is very well . . . X-Ray now shows a 25% diminution of density . . . We are greatly satisfied with the amelioration of this patient. I have seen many pleural effusions with a breast cancer. This is the first time that I have sent the patient home with such interesting results."

She was sent home on July 28, 1961. On March 3, 1962, her case history showed that she was continuing to receive Laetrile twice a week and that:

"It is to be stated that NO TOXICITY has ever been observed nor any side effects during this patient's treatment with Laetrile. Her general condition has greatly improved, the pain in her back of which she was complaining has almost completely disappeared. She is continuously gaining more energy, which permits her to perform her housework and going out shopping when necessary. A month ago she enjoyed a trip by bus to a carnival in Quebec City. This weekend she is going to a maple-syrup party in the country. Her weight for the last six weeks has remained at 120 pounds."

In the testing of experimental drugs, it is important that different scientists working in different places under different circumstances should nevertheless obtain similar results. This has occurred with Laetrile.

In New Jersey, for example, a 47-year-old woman who had her left breast removed subsequently developed metastases in the left armpit which broke down and caused foul odor and discharge. She suffered extreme pain throughout the chest and neck; her left arm was badly swollen. Surgery was impossible; Laetrile treatments were begun.

There was no apparent response to the first injection, but after the second injection the following day the pain and cough diminished and there was less discharge. Upon the third injection, the pain stopped completely and the

odor disappeared. As the treatment continued, the swelling of the left arm decreased, an indication that the cancerous action itself had decreased. Before-and-after analyses of the blood and urine showed definite improvement.* The woman was able to return to work and lead a normal life on a maintenance dosage.

Also in New Jersey was a boy, 17, who had lost 25 pounds over a period of three months. His skin was discolored; he suffered pain, weakness, nausea, and he had no appetite. On his neck a growth had developed, the size of one-quarter of an orange. The diagnosis was the cancer called Hodgkin's disease, granuloma type, with metastasis to the chest, and this was confirmed by biopsy. Because surgery was not possible, the boy was given Laetrile.

Two days after the first injection, the growth on the boy's neck had softened and decreased in size. By the fifth day, the growth was half its original size; it was now even softer and it was movable. The pains in the boy's armpits had stopped, and the swollen glands in these areas had diminished almost to normal size. His appetite was beginning to return.

Over a period of five months, the young man received 36 Laetrile injections—a total of 53 grams—and there were no side effects. He regained 24 pounds of his lost weight. He returned to high school, and upon graduation a few months later he passed the rigorous physical test of the Marine Corps and enlisted.

Elsewhere: in 1952, a California woman in her sixties suffered an attack which was diagnosed as colitis. When the condition worsened, X-Rays were taken and they revealed an intestinal constriction which was suspected of being a tumor. The woman's doctor recommended surgery and indicated that a colostomy might have to be done. In

* This test is described on page 98.

this operation, a generous portion of the intestines above and below the growth is removed and an opening is made in the abdomen for the discharge of waste material. The woman could not bring herself to undergo the operation and requested Laetrile.

During four months of treatment, all the symptoms of the illness faded and the woman appeared to be in good health. However, urine analyses indicated that a malignancy was continuing. Then one day the woman suffered an intussusception (one part of the bowel telescopes into another) and surgery was imperative. This gave the surgeon the opportunity to examine the area which earlier was suspected of being cancerous. A biopsy was done and cancer was identified. But the surgeon saw that the affected area was much smaller than the X-Rays had shown; he was thus able to remove it easily without resorting to a colostomy. Upon recovery, the woman resumed her Laetrile treatments. As of this writing, ten years later, the woman remains free of the disease. The effect of Laetrile in this case is particularly interesting: it caused the growth to regress to the point where it could be removed by simple surgery. Presumably, if the intussusception had not occurred, Laetrile would have regressed the growth completely.

Elsewhere: in Manila, a 56-year-old man developed a cancer of the nasopharynx (between the palate and the esophagus), with brain and neck metastases. When brought to the hospital, he was in severe pain, with vomiting and bleeding. The pain was relieved by the first Laetrile injection. After 21 injections at four-day intervals, the primary tumor had decreased to one-third its original size. The vomiting had stopped and the bleeding was down to a trace. Optimistically, the doctors planned to continue the injections, but the man felt so well that he went home and was not seen again.

Also in Manila, a woman of 32 was operated on in 1953

for a nasal polyp. The growth returned and required surgery the following year. In 1955, when the operation was performed for the third time, the growth was benign, but in 1956 it was malignant. She then underwent 16 radiation treatments, but the growth returned in 1957 and a fifth operation was necessary. This time, the radiation treatments were coupled with Laetrile. The growth recurred in 1958, again requiring surgery. Thereafter, Laetrile therapy was administered regularly. There was no recurrence of the cancer.*

To this list of Canada, the United States and the Philippines can be added Japan, England, Belgium, Italy, the Union of South Africa and Mexico. In these countries, Laetrile has remained on an experimental basis because of government requirements. But there have been exceptions. On July 4, 1962, the Krebses were notified from Iraq: "We have the pleasure to inform you that we have succeeded in registration of Laetrile with our Ministry of Health and we are now free to import this item." At the same time, news from Burma came that "the Army surgeons have found this product most satisfactory." The news was accompanied by a request for Laetrile for use in government hospitals.

Clearly, then, geography is no problem for Laetrile: it works everywhere. And there is something else distinctive about the drug.

If the occasion arose, there could be some debate about the Laetrile case histories: there could always be scientists who might say that the improvements in the patients were due to spontaneous regressions or the belated benefits of surgery and radiation, and the debate would get nowhere. But a debate on why Laetrile should—or should not—work would certainly reach a resolution because of the number of men—professors, researchers, specialists—

*See medical reports in Appendix for more extensive case histories.

who have the knowledge and experience to understand the body chemistry on which Laetrile is based and the physiological circumstances which make Laetrile necessary in the treatment of cancer. All that is required of such men is for them to use their knowledge and experience in order to achieve understanding. This sort of examination of ideas is a stern responsibility of scientists.

There is no mystery about Laetrile.

There need be no mystery about cancer.

The Krebses, father and son, have devoted their lives to that end.

put aside simply because the task of finding out was so great.

Krebs realized that the process of finding out would require more intensive study of certain sciences than were ordinarily included in the curriculum for a medical degree. He now had to decide whether to get his medical degree first and then do the special studying or to put his medical courses aside and get on to the special studies immediately. It was a difficult decision to make. As he pondered it, Krebs found himself growing increasingly convinced that Beard was right and that the special studies should be started at once. But what if, in the end, Beard turned out to be wrong? Many important years would be lost. The decision, therefore, was more than a matter of Beard's work: it was a matter of Krebs's life. Krebs finally decided that there could be nothing more important in his life than proving that John Beard was right because this would mean the conquest of cancer. He made up his mind not to return to medical school and he told his father. At first, Dr. Krebs was deeply disappointed.

"What are your plans?" Dr. Krebs asked.

"I think I'll go into research."

The doctor brightened. "Anything special?"

"Yes. Cancer."

"Why cancer, of all things?"

"Earlier this summer I read a book by John Beard and—"

"The Scotsman?"

Krebs was surprised. "Yes. Do you know him?"

Dr. Krebs nodded. "I remember reading some of his papers about 35 years ago, when I first began to practice."

Ernst Krebs then told his father how he had spent his summer, and in doing so he presented a resumé of Beard's theories.

Dr. Krebs said: "I remember now that, like everybody

else, I had my doubts about the trophoblasts, but I didn't think that there was something to Beard's ideas about enzymes. Come to think of it, that extract I made from apricot kernels was based on a premise not too remote from Beard."

"Yes, come to think of it," Krebs agreed.

Dr. Krebs sank back in his chair and regarded his son. "You're serious about what you want to do?"

"Yes, I am."

"All right, then you'd better get started."

Krebs started by transferring from Hahnemann Medical College to the University of Illinois where, for the next two years, he studied bacteriology and physiology, and this was followed by another two years at the University of California where he took extensive courses in anatomy and pharmacology. Throughout these years, Krebs continued his research on the Beard ideas. On weekends and vacations, he went to medical libraries across the country, poring through research reports in various science fields that were even remotely pertinent to what he called "*The Unitarian or Trophoblastic Thesis of Cancer*"—unitarian in that the trophoblast cell and the cancer cell were one and the same. Many of the papers Krebs found were in foreign languages, and to be able to read them he taught himself French, German, Spanish and Italian.

The aim of Krebs's research was to find confirmation of Beard's theory in the works of other scientists. Euclid, the Greek mathematician, had established the principle that two things equal to the same thing are equal to each other. Using this principle, Krebs hunted through scientific literature for clues that would link the trophoblast cell to the cancer cell on a basis of their similarities. He could not rely on what the cells actually looked like under the microscope. Cancer cells themselves vary greatly in size, shape and structure, and as a result of this many scientists believe there are various kinds of cancer. This

concept accounts for a great deal of confusion in cancer research and is responsible for holding the research at a standstill for years, despite the millions being invested in it.

The evidence which Krebs sought, therefore, was in the area of cell behavior and the chemistry involved. The task was enormous. There were hundreds of scientific journals being published every month and they had been published for years. They all had to be checked. Moreover, when Krebs found a pertinent article he also found a list of references at the end of it, and all these had to be checked. Sometimes two articles contradicted each other. To determine which was correct, Krebs had to duplicate the experiments in his father's laboratory. And sometimes two experiments, done by different men at different times in different places, actually complemented each other, and Krebs duplicated these tests, too, to be certain his own observation was right.

Nine years of university studies went into Krebs's research, plus an equivalent in time spent in libraries and laboratories. In 1947, after poring through 17,000 scientific reports, he was able to compile a list of 30 characteristics which the cancer cell and the trophoblast cell had in common, traits which no other cells possessed. Evaluated by the Euclidian principle, this was of the utmost importance.

Krebs released his findings to the science world, aware of the critical blasts that would ensue if he had made any mistakes. But there were no blasts. On the contrary, Krebs received several letters from scientists who felt he had put forth a fascinating idea. Encouraged, Krebs resumed his work, and soon he was able to identify 42 traits which cancer cells and trophoblast cells shared exclusively. This time, instead of publishing merely statements of facts on his findings, Krebs wrote a lengthy presentation of Beard's theory, brilliantly defining the trophoblastic

concept of cancer not only as John Beard had organized it but also as other scientists over the years had confirmed it by their own research without being aware that they were doing so. In 1950, the Krebs report was published in the *Medical Record*.

Once again Krebs sat back to await the blasts. Once again there were a few letters of praise.

And then there was silence.

CHAPTER 7

The Krebses had two hopes. First, they hoped that research experts would give the lengthy report about Beard's work a severe study, then admit that it was accurate or point out the errors in it. Second, assuming that there were no errors, the Krebses hoped some large pharmaceutical house with the necessary staff, equipment and funds would proceed to develop an anti-cancer drug based on Beard's pancreatic thesis.

Neither hope was fulfilled.

There could be any number of reasons why the Krebses' article in the *Medical Record* failed to stir much response. One thing was certain: if there had been any scientific errors in it there would have been a great deal of response. But perhaps its concepts were too revolutionary to be easily grasped. Perhaps they were too complicated. Or perhaps the problem was simply this: the scientists who read the Krebs paper already held such deeply entrenched personal opinions about the nature of cancer that they could not be dissuaded.

In any event, there was nothing the Krebses could do but continue their work alone and try to develop an anti-cancer treatment on the basis of the Beard theory.

According to Beard, pancreatic enzymes destroy trophoblasts. It thus seemed logical to inject enzymes to kill the cells when the pancreas failed to do so. By this time, the use of enzymes and hormones in therapy was common practice; insulin, the antidiabetic hormone, had been used as the treatment for diabetes since 1924.

Also by this time, scientists at the Rockefeller Institute in New York had succeeded in crystallizing the trypsin enzymes which Beard had said were effective against trophoblasts. Ernst Krebs, Jr., wrote New York and requested a supply of chymotrypsin, but he was told that the technique of extracting the enzyme from the pancreas of animals was so expensive and the yield so small that none was available for sale. In his own laboratory, Krebs went to work and devised an improved technique for producing chymotrypsin cheaper and in greater abundance, and he was shortly in the unusual position of providing the enzyme to the Eastern scientists who had pioneered the process in the first place.

The Krebses now began to use chymotrypsin on cancerous mice. From the start, they were able to observe distinct reactions in the animals, but the reactions were inconsistent. Although chymotrypsin was non-toxic, in itself it appeared to lack the force to do the job which Beard had attributed to it. The Krebses knew there could be various reasons for this. Perhaps not one enzyme but a blend of several of them was necessary to control trophoblasts. Perhaps the precise enzymes involved were still unknown. Perhaps as cancer progressed it produced a chemical resistance to enzymes. Or perhaps the chemical circumstances of advanced cancers required something more than enzymes. In any event, it was soon clear to the Krebses that chymotrypsin alone was not enough.

As he continued his research, Ernst Krebs, Jr., remembered the extract his father had made from apricot kernels. The extract had been effective to some degree on animal cancers, but an unidentified toxic factor in it had made it too dangerous for use on human cancers. Equipped now with a knowledge that had come from ten years of special studies, Krebs decided to experiment with the extract in an effort to track down the toxicity. Using the newest apparatus and techniques, he hydrolyzed

(broke up) the compound in his laboratory and discovered that the extract contained cyanide.

"No wonder the mice were dying," he told his father. "The cyanide was killing them."

Dr. Krebs thought silently for several moments, then said: "But there are still some questions. Why didn't all the mice die? Why did the cancers in some of them diminish, while in others there was no effect at all? When I tried to purify the extract it became less effective: was this because I had unknowingly removed the cyanide?"

There were many questions, and the answers could come only through further research. Krebs went back to his laboratory and to the medical libraries.

Beard maintained that Nature normally provided the means of preventing cancer in a properly functioning body. Krebs now faced the question: does Nature provide man with any means of controlling cancer in an improperly functioning body? There were realistic grounds for the question. Samuel Waksman, the discoverer of streptomycin, once said: "The cures for all of man's diseases already exist in the world around us. It is the task of science to recognize them through skillful research." Waksman himself proved this when he discovered in certain types of soil a species of microbe that produced an organic substance—streptomycin—which had the ability to destroy tuberculosis bacilli. It was reasonable, then, for Krebs to expect that Nature had provided similar defenses against cancer.

The months that followed were once again a period of scientific detective work for Krebs. He went over all the data he already had on the nature of cancer, then hunted for more, convinced that somewhere in chemical characteristics of cancer was the answer to the disease. As before, he read hundreds of reports by other scientists, correlating their findings with his own, duplicating their experiments for the sake of certainty, checking and

re-checking, slowly making progress, sometimes backtracking, occasionally going off on futile tangents, at times dropping an entire line of research when it proved worthless, but nevertheless steadily building a pyramid of vital facts.

He found, for example, that the enzymes called beta-glucosidases accumulated in great quantities in cancerous areas. Although this type of enzyme existed throughout the body, in cancer its presence was increased up to 3600 fold. In digestion, this enzyme helps to break down higher carbohydrates into lower carbohydrates. Krebs found that this enzyme was also able to break down his father's extract, releasing the cyanide. Thus he came to know the chemistry which had liberated the cyanide to do its lethal job on some of the laboratory mice.

But he knew something else: people ate small amounts of cyanide every day in various vegetables and fruits. Why wasn't this cyanide fatal to cells? Researching further, his attention was drawn to another enzyme, this one called rhodanese. Discovered in 1933, rhodanese was shown to have the ability to detoxify the cyanide which appeared in the body during the breaking-down of cyanide-bearing food substances. Then another discovery was made about rhodanese which turned out to be of the utmost importance to the Krebses' work: It was established that cancer cells were specifically deficient in rhodanese. In other words, cancer cells themselves had no defense against cyanide.

The next step was now clear to Ernst Krebs. He would have to change the molecular structure of his father's extract in such a way that the cyanide would remain firmly locked in the compound until it reached the abundant fields of beta-glucosidase at cancer growths. The enzyme would then trigger off the compound, freeing the cyanide which would proceed to turn on the defenseless cancer cells and kill them. If by chance any of the cyanide

escaped to the surrounding non-cancerous cells, the rhodanese would be there to detoxify it.

Equally clear to Krebs was the fact that once again Nature had provided man with the means of attacking another disease. With skillful research, Krebs had recognized the means. Now he would use the means to make the weapon. For the next months, Krebs experimented exhaustively with a general group of chemicals which in themselves were harmless but which possessed the capabilities of enacting the required processes, that is, releasing cyanide in the cancer areas, without injury to other tissue. He identified his specific compound as a *laevo-mandelonitrile-beta-glucuronoside*—Laetrile, for short.

He was ready now to see if his idea would work. He put some beta-glucosidase into a crucible and added some Laetrile. According to his calculations, the enzyme should trigger off the drug, releasing the cyanide. After a few moments, he held up the crucible and sniffed. He waited, then sniffed again. A thin trace of the pungent odor rose to him. He sniffed again. The smell was stronger now.

It worked.

At that moment, years of hard work reached their climax. The decade of struggles which began the day in 1938 when Krebs had first read John Beard now came to an end. The picture was complete. Scientifically, the cancer puzzle was solved. Krebs now knew the full cycle of cancer, from the appearance of the cancer cell by a coincidence of Nature to its death by Laetrile. The oldest disease known to man was now conquerable.

A wave of victory surged through Ernst Krebs and he inhaled deeply. Suddenly his legs went numb and his head began to spin. He realized what he had done: inhaling deeply, he had taken in an excess of cyanide gas.

He was on the verge of cyanide poisoning. Only a rush of oxygen could save him.

He put down the crucible and went quickly to the door and out into the garden, gulping air. He had to keep moving. He crossed the garden and went into the alley beyond and began running full speed down the block and back again, filling his lungs with air with each step. And as he ran he muttered over and over:

"It works! It works!"

It worked in the crucible, but now it was necessary to show that it worked on cancer cells—and safely. If while killing cancer cells Laetrile also damaged other cells, then it would be useless. Proceeding with his research, Krebs injected Laetrile into mice, increasing the dosage each day to determine if the mice had any toxic reactions to it. They had none. But what about human beings? There was only one way to find out.

Ernst Krebs took his life in his hands by preparing an injection of Laetrile for himself. He knew that there was more than enough cyanide in a single injection to kill him. And it would kill him if he was wrong about the defense provided by rhodanese. One thing was certain: one way or another, the Laetrile was going to be triggered off in his body. If he had cancer, the beta-glucosidase abundantly present in the area would trigger it off. If he did not have cancer, then there would be enough of the enzyme in his liver, spleen and kidneys to trigger off the drug. Either way, everything depended on the rhodanese. His research had indicated that, in normal tissue, wherever there was an abundance of beta-glucosidase there was also an abundance of rhodanese. Nature's defense pattern was clear: as the one enzyme liberated cyanide from compounds the second enzyme deactivated it. *And it was this defense pattern that would make Laetrile safe for use in humans.*

However, at the moment Krebs lifted the Laetrile in-

jection to his arm, this defense pattern was still theory. At the risk of his life, he was about to find out if it was fact. If he was right, he had nothing to worry about; if he was wrong, he would not be worrying for long. But he could not elude the test: he could not ask anyone else to take it for him. This was another of those moments in science that makes for heroes.

Krebs rolled up his sleeve and injected the Laetrile into his arm. He waited. A minute passed. Three minutes. Ten minutes. Thirty minutes. By now, he knew, the Laetrile was being carried through his system by his blood. Cyanide was being triggered off. And he was alive. *The defense pattern worked. Laetrile was safe for human use.*

For the rest of the day, he tested his blood and urine periodically, detecting in both the changes he expected to find. Everything had gone as he had anticipated. Laetrile was safe. It had performed in his body precisely as he had calculated. The challenge now was to prove that it would perform against cancer.



CHAPTER 8

Any new anti-cancer drug faces a grueling obstacle course. Before the drug can be used on humans, it must first be tested extensively on animals to establish that it has no harmful side effects. Further animal work must then be done to show that the drug does what its proponents claim. Regardless of whatever optimistic results may come out of these animal tests, the new drug is then restricted for a long time to hopeless terminal cases—patients in the last stages of the disease and for whom nothing more can be done by the conventional therapies of surgery and radiation. To be sure, there is a definite wisdom in these precautions: everything possible should be done to determine that the drug is harmless. But there is a definite futility in the prolonged restriction of the drug to terminal cases: the drug is required to prove itself on patients who are already practically dead. In other words, after surgery and radiation and time have reduced the patient to a shell of his former self, the drug is expected to bring him back from the grave.

There are other problems. Many doctors who will admit that there is nothing more they can do for a patient are nevertheless reluctant to use a new drug which has not as yet been approved by the Government or the medical profession. Even when it has been unquestionably demonstrated that the drug is harmless, the reluctance persists. And even when it has been unquestionably demonstrated that the drug is useful, the reluctance per-

sists. The reluctance would be understandable in early cases, when there is still hope that surgery and radiation might help, but in terminal cases, when all hope is admittedly abandoned, it is puzzling. Perhaps an explanation for it is that anti-cancer drugs are usually controversial—and they are usually controversial because they are outside the orthodox areas of surgery and radiation. Most doctors are far too busy to let themselves become embroiled in controversy, and the mere fact of the controversy could be enough to make them reluctant.

It is also understandable that doctors should look to the research leaders of their profession for decisions about new drugs. The leaders are experts; they presumably have the knowledge, facilities and time to make the decisions. But here, too, the new drug faces an obstacle. In order to make any research progress, a scientist must have some idea of the cause of a disease before he knows which direction to take in search of a cure. It is popular knowledge that there is little agreement among the leading cancer researchers as to the cause of the disease. Consequently, there are factions at the top of the profession. It is only human nature that the members of the various factions are cool to any explanation of cancer which contradicts their own, and any drug based on a contradicting explanation is unlikely to inspire any enthusiastic attention. The predicament becomes more complicated when it is remembered that these are the very men who make the judgments which greatly determine the treatments the general practitioner will use.

The Krebses were aware of these problems and knew they could not be easily overcome. However, rather than try to overcome them, the Krebses had enough confidence in the Beard theory to feel it could meet any tests, so they proceeded along the lines of the established pattern. Animal work and the injection Ernst Krebs, Jr., had taken had established that Laetrile was non-toxic.

Now more animal work was required to determine the effect of Laetrile on cancer cells. Early in this work, the Krebses observed a situation which in itself was no problem for them but which proved to be a stumbling block for other scientists who were later to test Laetrile on mice.

By careful breeding over many years, scientists have developed about 30 "strains" or "families" of mice in which it is possible to induce cancerous tumors by the application of the carcinogens. The process does not work all the time nor does it work in the same way all the time, but it works often enough to provide a steady supply of cancerous mice for laboratory experiments. But the supply from this source does not meet the demand, and so in order to provide more cancerous mice scientists have developed a technique known as transplantation. A malignant tumor from one mouse is cut into bits which are then embedded in other mice. If a number of uncontrollable factors happen to be right, the transplanted slivers of the cancer continue to live and grow. As with the carcinogenic process, this technique doesn't always work, but it works often enough to provide a greater number of laboratory animals.

In their work, the Krebses used mice with both types of cancers, and they wondered at first why Laetrile was having no effect on the transplanted growths. Then they realized that these growths were not "true" cancers in the Beardian sense. A "true" cancerous area would be permeated with a high concentration of the beta-glucosidases which would trigger off Laetrile. Having evolved in another body, a transplanted cancer was like an adopted child whose relation to its foster parents was legal but not lineal: the primary circumstances being different, the enzyme was not elicited from the hostal tissues and thus there was none of it to trigger off the drug. Upon establishing this, the Krebses stopped using

mice with transplanted growths. However, other scientists used such mice in their own Laetrile tests and, seeing no effects on the tumors, were discouraged from further investigation. Allies were thereby lost who might otherwise have made vital contributions to the work had they persisted.

The Krebses persisted. As the months passed, they repeatedly saw sloughs appear in the mice tumors; they even watched some of the tumors slowly vanish. Examining tissue, they observed the dead cancer cells. They found other necrotic matter in the blood stream, in the process of being eliminated.

Laetrile treatment of human cancers began in 1950, and it began slowly and carefully. The first injections, given intramuscularly, were only ten milligrams, administered every third day. Still to be determined in humans was the amount of cyanide that could be tolerated by the rhodanese enzyme; although mice had taken as much as a five-gram shot without effect, the method of treatment was so revolutionary that the Krebses decided to start with an injection that would be small enough to control but still large enough to demonstrate its action. The patients were Dr. Krebs's, and they were terminal.

The first reaction, noticeable in a few hours, was a decrease in pain. Patients no longer required as much narcotics as before; some were able to stop taking narcotics completely. This was extremely significant. In itself, Laetrile was not analgesic, although on hydrolysis it did release a small amount of benzoic acid capable of diminishing pain. Even so, the amount was too small to account for the consistent relief. The reaction, then, could only indicate that the pain-causing action had decelerated.

Feeling better, the patients experienced a return of appetite, with a subsequent gain of weight. Some who were bedridden became ambulatory. Others who had been given just a few days to live survived for weeks,

even months, and when they died most of them escaped the familiar excruciating cancer death.

The deaths were to be expected. Being terminal, the cases were already hopeless. Ernst Krebs put it this way:

"It cannot be said too often that in terminal-cancer patients a 'point of no return' is often reached before the first dose of Laetrile is given. This means that so much tissue has been destroyed, with the resulting metabolic alterations, that were every cancer (trophoblast) cell instantly and permanently destroyed, the patient's soma (healthy tissue) would not support life to the same extent afforded by an otherwise intact host. These definitely malignant trophoblast cells are not themselves noxious. When the patient enters the terminal phase of cancer, he enters it because the trophoblast has left irreparable structural damage—holes—in the soma. If one is shot by a steel bullet, he does not die from the toxic effects of iron."

In other words, a bullet kills because it causes fatal damage to vital organs. Cancer kills in the same way. In terminal cases, Laetrile destroys the cancer cells but it cannot create new cells, and if the vital host organ is already irreparably damaged then death will follow.

Despite the deaths, therefore, the Krebses were encouraged to go on. After all, a surgeon does not abandon the use of surgery because a terminal patient dies after he has performed surgery. For that matter, Laetrile was providing palliation (relief) for patients for whom the surgeons said nothing more could be done. The need now was for more patients, particularly patients whose conditions were not irreparably terminal. Certainly such patients were available in San Francisco, but doctors were reluctant to use a new drug, especially when they learned the active ingredient was cyanide. Repeatedly the Krebses explained the Beardian science on which Laetrile was based, but their professional friends failed to grasp it and remained negative. The Krebses turned to medical ac-

quaintances in Los Angeles and received a happier reception.

One of the first Los Angeles doctors to use Laetrile was Arthur T. Harris, a South African who had moved to the United States in 1928 and eventually settled in California in 1941. In the summer of 1951, Dr. Harris had returned to his homeland for a visit. He was then 57 years old and had a minor heart condition: the joyful reunion with his relatives and friends was all he needed to convince himself that he had worked long enough and ought to retire. When he got back to California, he persuaded his American wife and his two young children to move to South Africa. He sold his home and closed his practice and was about to leave the country when he heard about Laetrile.

The first aspect of Laetrile that caught his attention was that it was based on the science of John Beard. Harris had been a medical student at the University of Edinburgh from 1914 to 1919 and had studied embryology under Beard; he knew all about Beard's work with trophoblasts and, like others of the time, put it aside because there was not enough substantiation. Now, reading Ernst Krebs's writings, he recognized that the proof had been provided, and reading Dr. Krebs's case histories he recognized, too, that Laetrile offered great promise. He changed his mind about South Africa, bought a house and opened an office. He was unaware that his decision was to lead him to professional ruin.

Harris's first Laetrile patient was a divorcee of 36 who had a cancer of the cervix which had been established by biopsy (examination by microscope of a small specimen of the growth). Because she was planning to remarry and hoped to have children, she had refused treatment by surgery or radiation. Learning about Laetrile, she requested it from Dr. Harris. In December, 1951, the drug was administered locally into the ulcerated cervix and

intramuscularly in 20 to 40 milligram doses. Within a month, the woman had her first normal menstruation in several months, and examination showed that the previously eroded cervix was smoothly healed. A second biopsy was done and it was negative. The patient's personal physician refused to accept this biopsy and ordered a third done under his own direction, which was examined by his own pathologist. It was negative. Ten years later, Harris reported that the woman was still alive and free of any apparent evidence of cancer.

In the next 16 months, Dr. Harris treated 82 patients, and he reported:

Patients still alive and comfortable—24

Patients clinically free of cancer—3

Only temporary help—55

"Out of the whole series of 82 cases all were terminal cases except three. The terminal cases were cancer cases that had been subjected to one or more operations, to one or more courses of radiation therapy—X-ray treatment, radium therapy, cobalt bomb or radioactive injection therapy. All were doomed to die before they came to us: many of these are still comfortable and their cancers are 'clinically improved'. It is more than encouraging that so many incurables are not only alive but comfortable and active."

Harris's results were encouraging, indeed. When it is remembered that his patients were terminal, that they were on their death beds, even the temporary relief was remarkable. To be able to provide some relief from pain, to be able to extend life longer than the experts predicted, even to be able to allow for a subsequent death free of the cancer torment—these certainly were grounds for encouragement.

During this period of time, several more Los Angeles doctors began using Laetile, a group in New Jersey had taken on the drug, and it was being investigated by ex-

perts in London, Brussels, Turin, Manila and Tokyo, all of whom were obtaining results similar to Harris's. This widespread use was important in order to establish a pattern of reactions and to determine the proper regimen. It was found, for example, that injecting Laetrile intravenously brought clearer reactions than intramuscularly. And it was also found that the injections could be increased from ten milligrams to 400 milligrams with no harmful effects.

Meanwhile, Ernst Krebs, Jr., had succeeded in synthesizing Laetrile, thereby improving it vastly and assuring its constancy. The money to support the work continued to come from Dr. Krebs's practice and by 1952 it had reached a sum of \$200,000. Dr. Krebs was then 76 years old and unable to maintain his large practice. Previously, Laetrile had been provided free to doctors, but it was now clear that the work would have to pay its own way. When attempts to obtain grants from philanthropic foundations failed, doctors were asked if they would be willing to cover production costs of their supplies. Some of the foreign scientists were working at universities on budgets which did not provide for such expenditures and they continued to get Laetrile free, but the doctors in practice readily agreed to the suggestion.

It was also the agreement of the Laetrile doctors to keep their work quiet in order to prevent the panic that would certainly ensue if the news got out that a drug was available that appeared to have some palliative effect in cancer. There was still much to be learned about the drug. In fact, what the Krebses wanted most was to have a controlled study done at some large hospital where the pattern of Laetrile could be observed under the strictest conditions.

As the months passed, the number of Laetrile patients increased, and inevitably the news spread. And with the spreading news came controversy. Medical groups com-

plained that patients were risking their lives by refusing orthodox therapy in favor of an unknown drug which had never been properly tested and was not sanctioned by any authorized scientific agency. Dr. Harris repeatedly explained Beardianism and the Laetrile rationale to anybody who cared to listen, but both were rejected. In order to provide specific evidence for Laetrile, Harris decided that it would be a good idea to let the doubters see the results for themselves.

In November, 1952, Harris arranged a meeting at a Santa Monica hospital where the Chairman of the California Cancer Commission, a department of the California Medical Association, was invited to examine Laetrile patients. The meeting was inconclusive because the patients were not thoroughly examined and the opinion was expressed that either the patients had actually responded belatedly to previous treatment by surgery and radiation or that their tumors had undergone spontaneous regressions or that they never had cancer in the first place. Pursuing the matter further, Harris submitted all his reports to the Commission, complete with biopsies and autopsies. Krebs entered into a lengthy correspondence with the Commission Chairman.

Four months later on Monday, March 23, 1953, the Commission held a meeting in Los Angeles to which newspaper reporters were admitted. A long report was released in which the Commission indicated that a thorough investigation of Laetrile had been made with the conclusion that the drug was worthless, that it contained nothing to act against cancer cells, that it did nothing for the patients who had received it and that the science on which it was based was sheer nonsense. It was also said at the meeting that action would be taken against doctors who continued to use the drug. The report itself was subsequently published in *California Medicine*, the journal of the California Medical Associa-

tion, but that same day it was all over the Los Angeles front pages.

The report was devastating. One of its major criticisms was that Krebs was wrong in suggesting that cancer tumors contain a far great concentration of the beta-glucosidases enzymes than other parts of the body, that in reality the situation was the reverse. Actually, the idea of the abundant presence of the enzyme in cancer was not Krebs's. It was discovered by two leading scientists—Drs. W. J. Fishman and A. J. Anlyan—and reported by them in three different medical scientific publications* between 1948 and 1950. Krebs had merely utilized the discovery for the purpose of triggering off Laetrile in the cancerous areas, releasing the cyanide.

The Commission's report also said that a professor of biochemistry at the University of Southern California had blended some Laetrile and beta-glucuronidase in a bottle and inserted a strip of filter paper, the idea being that if any cyanide was released a discoloration would occur on the paper. But after 48 hours, the report said, there was no detectable trace of cyanide on the paper, and it was thus implied that the action did not occur.**

However, this finding was contradicted by a similar analysis that was being made at almost the same time in New York. The New Jersey doctors using Laetrile were perplexed by gossip reaching them about the California controversy. From the positive results they were obtaining, the doctors knew that Laetrile was achieving something, and when they heard that the Laetrile action was being questioned they decided to find out for themselves what Laetrile contained that made it function as it did. With this in mind, they submitted an ampule of Laetrile to Dr. Alexander A. Gettler, head toxicologist in the Office of the Chief Medical Examiner of the City of New

* See bibliography in Krebs-Bouziane paper, page 187.

** For a thorough test, see page 109.

York. Gettler was well known in the bio-analysis field.

In giving the Laetrile to Gettler, the New Jersey doctors were extremely careful not to tell him the disease for which the drug was intended. Gettler reported to the doctors on March 10, 1953. He said, first, that to save time he obtained a chemical diagram of the compound from associates of Krebs in California, and he included a sketch of the structure in his report.* Then he wrote:

"I then proceeded to check up this formula. There is no free hydrocyanic acid or free cyanide present. It is firmly bound in the molecule.

"I then hydrolyzed (broke up) the compound by boiling with HCl under a reflex. On testing for the components produced, I found hydrocyanic acid, glucuronic acid and an aglycon moiety which seemed to be benz-aldehyde. My analysis checked the formula given.

"The compound can also be hydrolyzed by the enzyme B glucuronidase found in malignant tissue, thus liberating the HCN at the site of the tumor.

"I hope this will answer your inquiry."

It did.

And the amazing thing about it was that, completely on his own, Dr. Gettler had linked the compound to cancer, describing exactly what the Krebses had defined as the Laetrile action: the cyanide was safely locked in the compound and could be released by the excessive presence of beta-glucosidase in cancerous areas. This directly contradicted the California report.

But the damage had been done.

* See page 154.



CHAPTER 9

Ethically, it is up to the individual doctor to decide what treatment his patient shall receive. The patient, of course, can refuse it, as many California cancer patients were refusing surgery and radiation in preference to Laetrile. Regardless of how other doctors or organizations might feel about this, there was nothing that could be done unless it was established that the preferred treatment was endangering lives. There was no such risk involved with Laetrile. The threat, therefore, that official action would be taken against doctors continuing to use Laetrile after its denunciation was actually contrary to medical tradition. After all, numerous medical practices—including the use of anaesthetics—had been denounced at their outset, only to be generally accepted later on. Aware of it or not, by leaving treatment decisions to the individual doctor, medicine was keeping the door open to the new ideas which had revolutionized science repeatedly over the years.

But this was now beginning to change in California. The threat of official action indicated that organized medicine was about to usurp the individual doctor's responsibility to do whatever he felt best for his patient. And matters did not stop there. Steps were taken to have a state law passed that would prohibit in California any cancer research which did not have the approval of an authorized committee. In other words, a scientist could not even do any laboratory cancer research without the permission of the committee. Even a cursory study of

medical history would have shown that there had been scarcely a single new idea in science which was not at first rejected by organized medicine, and it should have been clear that if a similarly restrictive law had been in general effect a century earlier medical standards would have remained at the level of the African witch doctor. Nevertheless, the law was eventually passed; versions of it were subsequently adopted by other states. If the intention was to protect the patient, one inevitable result was also the quarantine of scientific genius—which unfortunately has never been contagious.

Dr. Arthur T. Harris refused to be hamstrung by threats by medical leaders or laws. Convinced that the improvements he saw in his cancer patients were the direct result of Laetrile, he continued using the drug. He ran into new problems. Laetrile could not be used in hospitals; it became necessary to treat his patients in private clinics, in their homes or in his office. Not having his patients centralized, he had to do considerable travel, and this affected the number of patients he could see. It also affected him personally. After 16 months of Laetrile work, Harris reported:

"Of the total number of cases treated with Laetrile (82), 43 have been pay-patients and 39 free-patients. Of the 43 pay-patients many have paid only a part of their bills and much money has been written off on my books. Besides that, I have over \$5000 outstanding on my books at this time, and probably some 80% of this will never be collected. The net result is the fact that I am today mortgaged to the hilt, I have an unsecured loan at the Bank of America for \$2000 and unpaid current debts totalling over \$4000, whereas just 13 months ago I had not a mortgage or loan against me and had money in the bank. Apart from the inestimable satisfaction of trying to help my fellowman in evaluating this new and disputed

drug Laetrile, I am in bad shape and on the verge of complete insolvency."

In view of this, Harris was startled to receive, in September, 1953, a summons from the Los Angeles County Medical Association to appear for trial on October 12 for unethical conduct in overcharging three patients for Laetrile, thus allegedly displaying more interest in financial gain than in the welfare of the patients. Checking his files on the three cited cases, Harris was confident that the complaints would not hold up under cross-examination.

The first complainant was a widower whose wife had been a patient of Harris's. Files showed that the man had not paid a cent of the bills; they had been paid by the patient's parents. Harris telephoned the parents, who assured him that they believed Laetrile had prolonged their daughter's life and allowed her to die in less misery, that they were satisfied with his services and fees and would willingly say so at the trial. The second case was a man with Hodgkin's disease; because of the wide involvement, Harris had estimated that the man would require injections of four or five ampules. The man never returned for treatment: there had actually been no occasion to charge anything, let alone overcharge. The third case was a woman who was still concerned about a lump in her breast which had disappeared. Harris suggested a blood test; it was positive. To play safe, he suggested another test, but the woman did not return for it. Laetrile had not been used.

From all this, Harris deduced that the discussion at the trial would dwell not on these cases but on Laetrile itself and his continued use of it. This turned out to be true. At one point during the lengthy session, Harris asked: "Gentlemen, who is on trial here—Laetrile or me?" Prepared for this trend, Harris had brought along his case histories and several patients, but the hearing went

so far into the night that he insisted that most of his patients go home for their needed rest. By the time the trial ended at one-thirty in the morning, Harris noticed that several of the 22-man jury were asleep in their chairs. Harris subsequently reported:

"In closing, I told the Judiciary Committee that I would continue to use Laetrile as long as I got a case here and there that showed such remarkable results as the two I had presented. I would continue to use Laetrile until I got the final fully synthetic drug. Though that final Laetrile should be infinitely better than the present bio-synthetic (not fully synthetic) Laetrile, I would evaluate it. If it proved no good, I would report it as no good; if it proved to be good, I would so report it. I told the Judiciary Committee that, to date, Laetrile had ruined me financially, that now this Committee was gathered to take away my last asset—my good, professional name. I told them that, in spite of all this, I would continue to the end."

Two days later, Harris received notice that he had been expelled from the county medical society. He was given the right of appeal to the state association, which he made several months later. As a result, he was reinstated into the county society. But he never went back to it. Since he intended to continue with Laetrile, the whole thing would start all over again, and there was no sense to it.

Harris continued using Laetrile in California until 1957, during which time it became financially imperative for him to give up his home and move his family into a trailer. By now his professional position was unendurable and he had to make a decision to move elsewhere or starve. He decided to move—all the way back to South Africa. In 1958, he took a position with the Department of Medicine of the Natal government as supervisor of tuberculosis treatment in 41 hospitals affiliated with Christian

missionary stations. The work required a great deal of driving over the rugged African roads, and after two years of it Harris perceived that his heart condition was returning and he was forced to resign.

He joined the staff of a native hospital in Zululand. On February 23, 1962, he had the night duty. Early in the evening, he telephoned his wife to remind her that some old missionary friends were arriving the next day and would be guests in the Harris home, then he began his rounds of the hospital. Around ten, he was summoned to the delivery of a native woman, which turned out to be a breech birth. In the last minutes of the ordeal, the nurse assisting Harris observed that his eyes had become glassy. The baby was safely delivered; Harris spanked out its first scream of life, then he checked the mother to be sure she was all right. As the nurse left the room with the baby, she saw Harris back away and sink wearily onto a straight chair. When the nurse returned a few moments later, Harris was dead.

Arthur Harris's death deeply saddened those who knew of the sacrifices he had made rather than abandon his work under a great deal of pressure. But at least there was the consolation of knowing that, although separated from his co-workers by thousands of miles and a different way of life, he had kept in touch with the project and was aware of the progress that was being made. And the progress was vital.

The California denunciation and Dr. Harris's personal experience caused the Laetrile program to be severely curtailed. Several patients hotly insisted that they had been helped by the drug, but to little avail. The flow of new patients practically stopped. Doctors who were considering the use of Laetrile put it out of their minds; others who were on the fence about the drug got off; many who had reason to be encouraged by their early results decided to return to orthodox therapy. In years

to come, new doctors would learn about Laetrile and, understandably, they would make inquiries through official channels; back would come a copy of the California report; the doctors would shrug and look for something else for their patients. It seemed that as far as the United States was concerned, Laetrile was finished.

Under ordinary circumstances, Laetrile should also have been finished as far as the world was concerned. A powerful medical association had spoken, which should have been enough to silence everybody else. But this did not happen. The foreign scientists investigating Laetrile were beyond American censure. Moreover, they were men of such professional stature that they could not be called quacks just because they disagreed with an American authority. For that matter, they could not have cared less that the disagreement existed.

An example of this occurred in Brazil in July of 1954, at a time when the Laetrile controversy in California was still smouldering. The International Union Against Cancer, a bi-annual seminar of cancer specialists, was in session in Sao Paulo. One of the speakers was Dr. Ettore Guidetti, of the University of Turin, Italy. After presenting a resumé of the Laetrile science, Guidetti went on to speak of his own cases.

In order to observe the Laetrile action directly, Guidetti chose patients with terminal cancers of the uterus, cervix and rectum and with ulcerating breast cancers. He soaked tampons in a Laetrile solution and applied them directly to the growths and left them there for two or three days. He reported that the "destructive action of the glucuronoside on the cancerous tissue has been very net and in some cases one has been able to observe a group of fulminating and cauliflower-like neoplastic masses resolved very rapidly." He said: "The lytic (dissolving) effects produced by the Laetrile on the neoplastic tissue appear to confirm, consequently, the chemotherapeutic action of the

glucuronoside." Guidetti added that he had also injected Laetrile into patients with lung cancers, and he said: "I have been able to observe with the aid of radiography a regression of the neoplasm or the metastases."^{*}

A most interesting aspect of Guidetti's work was that for the first time Laetrile had been applied directly to cancer growths he could see without having to subject the patients to surgery. There had been criticisms that Laetrile had no effect on the growths, but now Guidetti reported that he had seen them dissolve with his own eyes.

When Guidetti finished, an American doctor rose and said that Laetrile had been investigated in the United States and was determined to be worthless. Guidetti said: "I do not care what was determined in the United States. I am merely reporting what I saw in my own clinic." The audience broke into applause.

Another important co-worker abroad was Dr. Manuel D. Navarro, professor of biochemistry and therapeutics at the University of Santo Tomas, Manila. At the very time Arthur Harris was being expelled from the Los Angeles County Medical Society, Navarro was addressing the University's medical association with these words:

"Since Hippocrates described a disease which we now know as cancer, various groups of oncologists have striven to discover a drug for the treatment of this scourge of mankind. The long years have brought to light innumerable drugs claimed to have incredibly dramatic effectiveness against this disease, which, however, were proven later by controlled experiments as palliative only, if not worthless. 'Advances in medicine,' it is said, 'are like salesmen knocking at your door. Hear them before you dismiss them.' As a student of biochemistry and oncology, I have ventured, therefore, to knock at your portals to bring to your kind attention and tolerance another of

^{*} "Preliminary Observations of Cancer Cases Treated With a Cyanogenetic Glucuronoside," ACTA, Vol. XI, No. 2, 1955.

these wonder drugs: Laetrile, a synthetic drug discovered by Ernst T. Krebs, Jr., which to my mind, training and experience is *the ideal drug for the treatment of cancer.*"

Navarro proved valuable to the Laetrile project in many ways. He was, first of all, fully qualified to evaluate the drug. He had excellent facilities available for his tests. Patients were plentiful. Also, because of his eminent position in cancer research, he had to be listened to when he spoke. And in addition to speaking, he wrote. Scarcely a year passed once he began his work without a Laetrile article by him in major scientific publications.* Thus Navarro produced a panorama of the Laetrile progress over the years. He had joined the work at the beginning, when the team was small and there were only glimmers of hope, and his own research not only helped build the pyramid of confidence in Laetrile but also attracted other scientists to the steadily growing project. He also contributed importantly to the development of a test which was to give medicine its first weapon in an area crucial to the survival of cancer patients: early diagnosis.

In 1927, two German scientists—Ascheim and Zondek—observed that when they injected extracts of the urine of pregnant women into female mice or rats the animals were stirred to sexual heat. This led to the A-Z pregnancy test and was the basis for practically all subsequent pregnancy tests. Experiments by others identified the active substance in this case as the human chorionic gonadotrophin hormone (HCGH). At the time, it was believed that the embryo produced the hormone for metabolic purposes. An article then appeared in the *Journal of Experimental Medicine* by Dr. C. E. Cori to the effect that this same substance had been found in the urine of cancer patients. This was confirmed by other scientists. In 1944, Dr. A. Roffo, working in Argentina's

* See bibliography.

Institute of Experimental Medicine For the Study and Treatment of Cancer, reported that he had found the hormone in 100% of 1000 cancer patients and did not find it in 100% of 1000 people who did not have cancer.*

A stumbling block was that it had been established that the pituitary gland produced a gonadotrophin hormone; many scientists then deduced that the source of the hormone both in pregnancy and in cancer was the gland. However, in 1946, Ernst Krebs, Jr., and Dr. Charles Gurchot succeeded in isolating HCGH from the urine of males with extra-genital cancers and demonstrated it to be chemically and physiologically different from the pituitary hormone. The HCGH, they found, was broken up by the pancreatic enzyme chymotrypsin, whereas the pituitary hormone was not. It was important to remember that, according to John Beard, chymotrypsin also destroyed trophoblast (cancer) cells. This was also important: the pituitary gonadotrophin was normally present in human urine, but HCGH was present only in pregnancy and cancer. Consequently, it could only be adjudged that a single factor was involved in both situations. According to Beardians, this single factor was the trophoblast cell, functioning normally in pregnancy and functioning abnormally as cancer.

And this, too, was important: in pregnancy, the amount of HCGH in the urine of pregnant women rose steadily until the fifty-sixth day, when it declined sharply until it was scarcely detectable. In the urine of cancer patients, on the other hand, the HCGH factor rose steadily and kept rising until death.

And this was vital: when Laetrile was injected into cancer patients the HCGH factor declined.

On the basis of these developments, Dr. Howard H.

* "Tumoral Gonadotrophic Hormone In Cancerous Patients," Boletin de Instituto de Medicina Experimental, Vol. XXI, No. 65, 1944.

Beard,* formerly of Yale and the Chicago Medical School, devised a test which not only readily established the presence of HCGH in a urine specimen but also measured the quantity in a way that gauged the extent of any cancerous action. The test proved to be 95% accurate. In Manila, Navarro made slight modifications in the test and raised its accuracy to 97%. In the July-August, 1957, issue of the *Santo Tomas Journal of Medicine*, Navarro, reporting on 42 cases, said:

"The Beard Anthrone Test, which is a test for the by-product of the cancer cells, the chorionic gonadotrophin, is a micro-Ascheim-Zondek test. It is used for the diagnosis of early pregnancy and malignancy of all types. In this study, four surgical biopsies have been found negative for malignancy yet these cases were all positive to the Beard Anthrone Test. Autopsy or laparatomy much later proved that the Beard Anthrone Test was accurate in the earlier stages of the malignant process. In this series, a 97% accuracy was obtained. This test seems to be an excellent gauge of the response to the effectiveness of the treatment given to the cancerous patient.

"That this test would come in very handy when no tissue or exfoliated cells are available to be sent to the pathologist for histological examination is obvious; moreover, when radiography casts doubt on a diagnosis of malignancy, the use of the Beard Anthrone Test would certainly aid greatly in the solution of the diagnostic difficulty."

Something more could be inferred. When the Beard test is perfected to 100% accuracy, it will be possible to detect cancerous action in its very first stages. Thereafter, people need go to their doctors just twice a year to have their urine analyzed: if any HCGH is found in any men and in non-pregnant women, they need merely take

* No relation to Dr. John Beard.

Laetrite injections to kill the active trophoblasts which are producing the hormone. By regular analyses and regular Laetrite injections, the cancer need never go beyond that early stage.



CHAPTER 10

After ten years of Laetrile work, the nature of cancer has become increasingly clear. In the strictest sense, it is not a disease. It is a condition. Everybody is implicitly susceptible to it because of the pre-cancer cells—the diploid totipotent cells—which are scattered throughout the body during early fetal development. Should these cells (and there are probably millions of them in the human body) ever be acted upon by the sex hormones (estrogens), they undergo cell division which turns them into trophoblasts—cancer cells. Chances are that most people actually have cancer more than once in their lives—but only for as long as it takes for the pancreatic enzymes to arrive at the scene and destroy the cells. It is when the enzymes fail to appear that the cells multiply and the condition known as cancer develops.

And here is the heart of the matter: removing a cancerous tumor by surgery or burning it with radiation or even destroying the cells with Laetrile does not change the basic situation. Unless the pancreas is repaired, the cancer cells still in the body will continue to reproduce, and even if all cancer cells are destroyed the condition will recur the next time estrogens act upon other diploid totipotent cells.

Therefore, there can be no such thing as a former cancer patient.

As with diabetes, which also involves a faulty pancreas, a person who has cancer once will remain subject to it as long as the pancreas remains faulty, usually for life.

The idea of a cancer cure, then, is inaccurate.

The idea of a cancer control, on the other hand, is perfectly plausible.

In the minds of an increasing number of leading scientists, the best control now available is Laetrile.

To be sure, this concept appears to conflict with the "cures" claimed by some surgeons and radiologists with patients in whom the disease did not recur during the five-year danger period arbitrarily established by the medical profession. However, all that has actually happened with these cases is that the cancerous area was subjected either to radical surgery or radiation before the active trophoblasts had a chance to spread. If the disease has not recurred, it is only because the organizing factors have not recurred: the tissue damage did not occur again which would send estrogens against other diploid totipotent cells elsewhere. In this light, surgery and radiation, then, are treatments for one of the symptoms of cancer—the growth itself—and even when they are effective against an isolated growth they nevertheless do not change the circumstance which allowed the trophoblasts to multiply in the first place: the faulty pancreas.

Medical science concedes that radiation, even when effective against cancer, is also harmful in that it also destroys the surrounding healthy tissue, sometimes to the extent that the host organ cannot function properly thereafter. For this reason, Beardians frown on radiation. Surgery, however, retains a role in Beardianism. It is established scientific fact that when cancer (trophoblast) cells begin to reproduce by rapid division the surrounding somatic cells also reproduce at an increased rate in a seeming effort to localize the malignancy. Therefore, a cancer tumor contains somatic cells as well as cancer cells: the larger the tumor the fewer the cancer cells, and the reverse of this is also true.

Laetrile acts only upon cancer cells, with the result that

when all the cancer cells are destroyed there is still a tumor—but it is now benign. Beardians recommend that once it has been established by the Beard Anthrone Test (or its forthcoming perfected successor) that the malignant action has ceased, the surgeon should remove the benign growth in order to grant the patient relief from the discomfort. As a precaution, the affected area should be treated directly with Laetrile during exposure.

All of the currently suspected causes of cancer fit into the Beardian explanation. Can smoking cause cancer? In tobacco smoke are tars capable of damaging lung tissues in a way that elicits estrogens to stimulate repairs; if diploid totipotent cells are in the area and undergo division, the development of cancer will depend on whether the pancreas is able to provide the enzymes to destroy the cancer cells which appear on the second division of the diploid totipotent cells. Viruses? The tissue damage done by viruses evokes the same estrogenic flow, producing the same situation, with the same risks and the same defenses—or the same lack of defenses. It should be stressed, however, that tobacco tars and viruses do not *cause* cancer: they *organize* it. What about injury or prolonged physical irritation or regular exposure to known carcinogens like coal dust or radiation? These, too, can be “organizers.” Can cancer be the result of abnormal changes in a cell? No. No body cell can of itself change into anything it does not possess the inherent qualities to become. The only body cell with the inherent quality to become a cancer (trophoblast) cell is the diploid totipotent cell. Are there different types of cancer? Only superficially. The technical names given cancer growths describe where they are located, their virulence and the appearance of the cell under the microscope, but the malignant component is always the trophoblast cell. This cell has the faculty to disguise itself due to environmental circumstances, and thus takes on a variety of appearances,

but intrinsically it is the same cell whatever its appearance, just as a Negro, Chinese and Caucasian, though differing in appearance, are intrinsically the same creature: Man. The "multi-disease" concept of cancer is a familiar medical error that was once held regarding tuberculosis, pneumonia, even appendicitis. Time and study proved this concept wrong in these diseases; time and study will prove it wrong in cancer.

The Krebses steadily continued giving time and study to Beardianism and Laetrile therapy. Working with them over the years was Dr. Charles Gurchot, the professor who, in 1938, urged Ernst Krebs, Jr., to determine for himself whether or not John Beard's theory about the trophoblastic nature of cancer was correct, and thus sent the young man off on research that changed his life. Gurchot was among the first to be persuaded by Krebs that Beard has indeed been right. Subsequently Gurchot and Krebs performed experiments to confirm their convictions and co-authored scientific reports on their tests. Thus, for twenty-five years, the professor and the student have remained co-disciples of the Scottish embryologist they both at first had doubted. In honor of the Scotsman, they organized the John Beard Memorial Foundation for the purpose of promulgating his ideas.

During most of these years, the work had been severely curtailed in the United States, but the progress of the foreign investigators was persistently encouraging. From Maisin in Belgium and Bodman in England* and Guidetti in Italy and Navarro in the Philippines and Saki in Japan came a steady stream to Krebs of case histories attesting that Laetrile was doing its job. With each man, the pattern was the same: in terminal cases, Laetrile was an effective palliative; in earlier cases, it inhibited the

* John Bodman, leading British researcher, died in 1962. Joseph Maisin is director of the Cancer Institute, Louvain University.

rowth and there was evidence of regression. Navarro went so far as to describe Laetrile as "curative" in early cases on the basis of negative Beard Anthrone Tests, but his co-workers agreed that because the test was still not accurate to the most minute degree and because the pancreas remained faulty the description could not be accepted as definitive. Doctors asked: "When does my patient stop taking Laetrile?" The answer: "He doesn't, any more than a diabetic stops taking insulin, but when you, as the physician, are satisfied that the danger is over the patient can cut down to a maintenance dosage in amounts required by his condition, perhaps merely to a brief series of injections at the time of his regular check-ups."

In addition to his own research, Ernst Krebs, Jr., was kept busy answering such questions and correlating the reports arriving from abroad. His work still required him to travel considerably. Late in 1958, he was in Miami, and friends suggested that there was another visitor in town he should meet: Andrew R. L. McNaughton. This incidental encounter proved to be an important turning point in the Laetrile development.

A consulting engineer, McNaughton is a son of General Andrew G. L. McNaughton, commander of the Canadian forces during World War II, formerly president of the National Research Council of Canada and the Chairman general of the International Joint Commission. During the war, the younger McNaughton was chief test pilot and officer commanding the Experimental Test and Development Establishment of the Royal Canadian Air Force, subsequently becoming an international engineering consultant at government levels. He is also founder and president of The McNaughton Foundation, sponsors of independent research.

McNaughton had heard about Krebs and Laetrile and, based on what he had heard, had accepted the California

Cancer Commission's evaluation of both. However, having a personal background in research and having been raised in a home where leading scientists were regular dinner guests and the problems of scientific research were taken seriously, McNaughton was a perceptive audience when Krebs told him the full story. McNaughton decided that quite likely the California evaluation had been premature. He asked Krebs to send copies of his writings to The McNaughton Foundation office in Montreal. Upon reading the papers, McNaughton realized that they belonged in the hands of a qualified scientist. He presented them to Dr. N. R. Bouziane, professor of pathology and biochemistry at the University of Montreal, dean of American College of Bio-analysts and Director of Research Laboratories and Chemotherapy Specialist of Tumor Board at Montreal's famed Hôpital Ste. Jeanne d'Arc.

Bouziane later said: "When you have spent your life in research, you pick up a lot of 'excess baggage' which you can't use at the moment but hope will prove useful later on. It so happened that when I read the Krebs paper I had the 'excess baggage' to grasp the Beardian theory immediately and to recognize its value."

To benefit from a variety of opinions, McNaughton circulated the Krebs papers to other Canadian scientists including Dr. Jacques Daneau, of the Canadian Radiological Institute. The opinions were all the same: the subject was interesting and worthy of further study. A few months later, arrangements were made for a Canadian investigation of Laetrile under The McNaughton Foundation's sponsorship. Government permission was necessary to use the drug in hospitals; McNaughton requested and obtained it. At the same time, McNaughton set up a channel of communications from his office to the pertinent government, medical and scientific organizations in order to keep them informed of developments, and

agreed that the work should be done without publicity in order to prevent spreading false hopes or eliciting criticisms left over from the California evaluation. The Canadian work began in mid-1960 and continued quietly for two years, by which time Laetrile was being used in 10 hospitals in Quebec Province.

From the start, the results were the same as they had been in other countries. The important difference was the scope of the work. Though working independently of each other, the score of Canadian doctors nevertheless comprised an impressive team. Discussions of Beardianism and Laetrile were held at both McGill University and the University of Montreal. Krebs was summoned to Montreal to answer questions put to him by a symposium of Canadian specialists. From this meeting, the subjects of Beard's science and Laetrile moved into the classrooms of McGill University and the University of Montreal where they were presented to the future doctors of Canada.

Having observed the palliative effects of Laetrile in terminal cases, one Canadian doctor after another urged that the necessary steps be taken to obtain government approval for qualified investigators to use Laetrile on early cancers. It was apparent that the time had come for similar steps in the United States as well. Krebs prepared a lengthy report on his work, which was submitted to both the American and Canadian FDAs late in 1962. As of this writing, neither agency has responded. However, in view of the new FDA regulations, passed by Congress in late 1962 as a result of the Thalidomide scare, the American response, at least, will be slow in coming because of the additional red tape involved in the new procedures.

But there have been developments in other areas. In September, 1960, Krebs received a letter from Dr. D. R. S. Kirby, an embryologist at Oxford University, who wrote:

"May I say how interested I am in the view put forward by you and your colleagues in your paper "The Unitarian or Trophoblastic Thesis of Cancer." I am attempting to simulate or rather produce extra-genital chorioepitheliomas experimentally by transplantation techniques, with very interesting results. The results so far fully corroborate the Unitarian Theory."

Kirby's corroboration of the scientific work done by Beard and confirmed by the Krebses was extremely important. To have a man of his professional stature announce his conviction that the trophoblast cell and the cancer cell are one and the same would certainly capture world attention.

In May, 1962, Kirby published in *Nature*, a British science journal, a report on an experiment he had done with trophoblasts. He extracted cones of trophoblasts from the uteruses of pregnant mice and implanted them into the mammary cancers of other mice. A few days later, he saw that the trophoblasts had caused erosions to occur in the tumors, and he also saw that cancer cells in the eroded areas had been destroyed. This led Kirby to entitle his article "Ability of the Trophoblast to Destroy Cancer Tissue," and he suggested that perhaps trophoblasts might be used in an injection for the purpose of destroying cancer cells in a malignant tumor.

The mere fact that trophoblasts were being linked to cancer by an important scientist in an important journal was a great step forward for Beardianism. However, suggesting that trophoblast cells could destroy cancer cells, Kirby was suggesting—in Beardian terms—that trophoblast cells could destroy trophoblast cells, since trophoblast and cancer cells are one and the same. In reply, Krebs prepared a question-and-answer statement (see page 245) in which he explained that this type of cannibalism was unlikely. He pointed out that 90% of the cells in a mammary tumor are benign and he said that

these were the cells which Kirby's transplanted trophoblasts were destroying. Kirby said he found dead cancer cells in the cavities made by the trophoblasts. This occurred, said Krebs, because the malignant action already going on in the tumor was so violently increased by the transplanted trophoblasts that any hostal malignant cells in the path of the transplanted malignant cells were destroyed ineluctably by the accelerated necrosis. Therefore, the destruction of cancer cells already in the tumor was accidental: they just happened to be in the way. By the implantation of trophoblasts, the tumor actually became more malignant than it had been before and it would now continue progressively so.

There was a significant sidelight to the Kirby experiment. For years, Krebs had insisted that doctors interested in using Laetrile should first be thoroughly indoctrinated in Beardianism. Krebs argued that Beardianism and Laetrile could not be divorced, that actually Beardianism was more important because it provided the scientific basis for the drug and that unless a doctor knew what to watch for in the patient he would not know how to use the drug properly. To assure a complete understanding of the science, Krebs was therefore always ready to go to any extent to clear up misconceptions which inevitably popped up.

Another such instance concerned the fundamental mechanism of Laetrile. Doctors repeatedly asked Krebs if there was some way he could demonstrate the Laetrile action in the laboratory in order to assure once and for all that it actually occurred. In the summer of 1962, Krebs devised a brilliant test expressly for this purpose.

He acquired a quantity of daphnia—ordinary water fleas—and several aquaria of the type used by people who raise tropical fish as a hobby. Into a tank of water at room temperature he placed some of the daphnia, then added Laetrile in a concentration equivalent to a three-gram

injection in a 150-pound person. He examined the tank 24 hours later and found that practically all of the daphnia were still alive. He repeated the test, but this time he added crystalline beta-glucosidase in a concentration much less than occurs in cancer. The enzyme crystals triggered off the Laetrile, releasing the cyanide, and in five minutes most of the daphnia were dead. He repeated the test again, but this time he boiled the beta-glucosidase before adding it to the tank, with the result that the boiling of the enzyme rendered it incapable of triggering off the drug. When he put the boiled enzyme solution into the tank, nothing happened to the daphnia. But when he then added the regular enzyme the daphnia were dead in two or three seconds. Removing the dead daphnia, Krebs boiled the solution under a hood, causing distillation of the cyanide. Letting the solution cool to room temperature, he added more daphnia. Twenty-four hours later the fleas were still alive because there was no cyanide in the water to kill them.

Then Krebs took the next step. Again he prepared the Laetrile-enzyme solution, but this time he added rhodanese in the presence of a trace of colloidal sulfur and incubated the mixture at 37 degrees Centigrade with slight agitation for 24 hours. He let the solution cool, then added the daphnia. They remained alive indefinitely because the rhodanese had detoxified the free cyanide in the tank. As the next step, Krebs boiled the rhodanese. This time the daphnia died because the rhodanese had been inactivated by heat denaturation and thus there was no defense against the cyanide. As a final step, Krebs again prepared the solution of Laetrile, beta-glucosidase and rhodanese, but now he added chorionic gonadotrophin hormone. After incubation, agitation and cooling, he put the daphnia into the tank. The HCGH had inhibited the rhodanese and all the daphnia were dead in five minutes.

In effect, Krebs had duplicated the architecture of cancer, reproducing the checks and balances which Nature provided both to protect the trophoblast cell and to destroy it. In pregnancy, the protection was essential until the umbilical cord matured, then Nature normally provided the destructive pancreatic enzymes in sufficient quantity; outside of pregnancy, it was the failure of the destructive enzymes to appear in quantity that allowed the cells to proliferate as cancer. As a result of Krebs's experiment, any scientist could now demonstrate the chemical action in his own laboratory for his own satisfaction.

There was another result to this experiment. Some weeks after receiving a report of Krebs's experiment, Andrew McNaughton spent an evening reading in his Montreal home. He came upon an advertisement by a major pharmaceutical company which discussed a disease called "snail fever." Known scientifically as schistosomiasis or bilharziasis, the disease is caused by tiny parasites which breed on the bodies of snails which inhabit practically all of the rivers and lakes of Africa. About 100 million people suffer from the disease—half the people on the enormous continent. The disease arises when the parasites pierce the skin of people, enter the blood stream and are carried to vital organs where they cause steadily progressive damage which gradually destroys the organ and can cause death. The most prevalent result of the disease, however, is blindness, and it is evident everywhere in Africa.

Remembering Krebs's experiment in which liberated cyanide killed daphnia, McNaughton wondered if the same Laetrile mechanism could be aimed at the parasites in snail fever. He put the question to Krebs. A few weeks later Krebs replied that the question had once more sent him back to his books and he discovered that John Beard himself had predicted years earlier that the larval forms

of the parasites should be amenable to crystalline pancreatic enzymes. He wrote McNaughton:

"I would be surprised, indeed, if Laetrile failed to be of great value in schistosomiasis. Of all the stages, I would guess that Laetrile might be most valuable at the adult stage because here is a multicellular parasite equipped with a comparatively complex digestive apparatus that in all probability carries high quantities of the beta-glucosidases. Offhand, I see no evolutionary reason why this organism should be equipped with a rhodanese mechanism to deal with Laetrile. There is not only the probable endogenous beta-glucosidase; we know with certainty that the presence of the organism stimulates a beta-glucuronidase response in the focus of parasitization in the host. The idea of the relevancy of Laetrile here was brilliantly conceived. The idea is so very, very good that one could not pass it by without testing it."

McNaughton showed the letter to Dr. Bouziane, who said: "Yes, he's right. Laetrile should destroy the parasites. But I don't know how we can do any tests. I never heard of anybody in Canada who had snail fever. You'll have to go to Africa."

McNaughton assured that when the time came he would, and he realized that if Laetrile did prove to be effective against snail fever it should also be effective against other parasitic diseases, like malaria, for example. A whole new world would open for the drug.

And the cancer world is already opening to it more and more.

In January, 1963, the Sloan-Kettering Institute for Cancer Research indicated in its annual progress report that the fast developments in cancer research might lead to a "Unifying Concept" on how cancers are formed. This concept was already available; it was called Beardianism and was defined by the Krebses in 1950 in their report.

"The Unitarian or Trophoblastic Thesis of Cancer," in the *Medical Record*.

Also in January, 1963, the *Journal of The American Geriatrics Society* carried an article that was distinctly Beardian. Its title was "Beta-Glucuronidases: Their Significance and Relation to Cancer," and it was written by Dr. Mihaly Bartalos and Dr. Ferenc Gyorkey, of The Johns Hopkins University School of Medicine. Part of their work was supported by a grant from The American Cancer Society. The article is a correlation of the work already being done on the subject by leading scientists. Prominent in the article is a reference to Navarro, the Philippine Beardian, and the trigger action of beta-glucuronidase upon Laetrile is described. Listed in the bibliography is Navarro's 1957 *Journal of the Philippine Medical Association* report, "The Mechanism of Action and Therapeutic Effects of Laetrile in Cancer." In their conclusions, the two Baltimore scientists state that, on the basis of their work, a relationship between cancer and beta-glucuronidase can be justifiably assumed. This directly contradicts the 1953 California report.

At about the same time the first account on Laetrile patients appeared in an American medical journal. This was the report on ten cases by Dr. John A. Morrone, attending surgeon at the Jersey City Medical Center, in *Experimental Medicine and Surgery*.^{*} Morrone had learned of Laetrile through Andrew McNaughton, a personal friend. The first aspect of the work that had caught his interest was the 1953 Gettler letter to the New Jersey doctors, which said that Laetrile would release cyanide at the site of the cancer. Morrone knew Gettler personally, had worked with him in the past and greatly respected his judgments.

On the strength of this, Morrone decided in 1960 to

* See page 205.

go to Montreal and discuss Laetrile with Dr. Bouziane. It so happened that Krebs was in Montreal at the same time. The two men met and spent three days discussing Beardian science. Morrone was impressed by Krebs's habit of citing the research source for the various substantiations of Beardianism. During a break in the discussion, Morrone went to a medical library to check out some of the reports Krebs had quoted. He found them all. He also found Krebs himself—poring through new scientific journals in his endless quest to find more and more confirmation of Beardianism.

Returning to New Jersey, Morrone began using Laetrile on his terminal patients. In his subsequent report he described the familiar pattern of reaction: decrease in pain, return of appetite, gain in weight, improvement in general condition, some degree of return to normality, all of which, he reported, suggested a regression of the lesion. He also observed, as others had, that terminal cases, at least, required continued treatment in order to sustain their response.

The tremendous importance of Dr. Morrone's report was that it was the first positive statement to be made for Laetrile in an American medical journal. In effect, the Morrone paper released Laetrile from the American prison where the 1953 California report had put it. Doctors who had been dissuaded from using Laetrile because of the California evaluation could now reconsider the drug in a new and positive light.

Thus, as 1963 progresses, it becomes evident that the time has come for an American re-evaluation of Beardianism and Laetrile at the highest scientific level. This has previously been difficult to arrange because of the lingering devastation of the 1953 California report and the reluctance thereafter of the Krebses to subject themselves to more of the same. But now the situation has changed considerably. Positions of professional leadership

are now filled by men who had not been part of the earlier controversy: as scientists, they can review the work with open minds.

Only a few things remain to be done. A conference is necessary between Beardians and other scientists who possess the extra knowledge which Bouziane once described as "excess baggage." There can be only one outcome to such a conference: agreement that cancer is a Unitarian disease. On the basis of this agreement, it should follow that Laetrile, already dramatically demonstrated as palliative in terminal cases, should be given an opportunity to demonstrate itself on early cancers.

The Krebses feel that their work can survive the most thorough scrutiny. Ernst Krebs, Jr., has said: "The Beardian explanation of cancer is irrefutable. Any other explanation of cancer reduces itself to an absurdity. If anyone can prove that cancer is not trophoblast, I will put aside all my work, including Laetrile."

Dr. Bouziane has said: "Laetrile must await the test of time. We have found that Laetrile is a powerful tool against cancer. As clinicians, it is up to us to find ways to enhance its therapeutic action and to exploit all its potentialities."

Andrew McNaughton has put it another way. "The evidence accumulated by our medical advisers convinces us that if Laetrile is used in early cancers there need not be terminal cases," he has said. "And when proper diagnosis is available to identify cancer in its pre-tumor, pre-clinical stages, we can confidently expect that Laetrile will remove even the dread of early cancers from our lives."

This has been the lifelong goal of the Krebses. It is the hope of the world.



APPENDIX

The following medical reports, case histories and questionnaire are provided for doctors and researchers who desire a review of Beardianism and Laetrile at the scientific level. Professional comments and inquiries are invited by The McNaughton Foundation, Suite 900, 2015 Drummond Street, Montreal, Canada.

THE UNITARIAN OR TROPHOBLASTIC THESIS OF CANCER*

by Ernst T. Krebs, Jr., ** Ernst T. Krebs, Sr., †
and Howard H. Beard ‡

It is veritably impossible to find, among the hundreds of valid experimental contributions to our knowledge of cancer made during the past half century, an experimentally established datum that would contravert the thesis of the basic biological uniformity characterizing all exhibitions of cancer.

THE CRITERIA OF UNIFORMITY

To the experimentalist who does not overtly accept an unitarian thesis of cancer, such a thesis is still implicit in the commonplace facts of his science. The classic experiments of Warburg on the respiratory pattern of cancers of various species and tissue origins reveal a high uniformity from tumor to tumor.¹ Correlatively, the Coris find the lactic acid and sugar content of the various exhibitions of cancer to be highly uniform.² Williams and his co-workers report a pronounced degree of uniformity in the concentration of eight B vitamins in a great variety of animal and human tumors, regardless of the tissue of their origin or the manner of their induction.³ Robertson makes similar observations for vitamin C.⁴ The addition of various substrates to malignant tumors of various types yields highly uniform respiratory responses.⁵ Shack describes an almost complete uniformity in cytochrome oxidase content in a number of mouse tumors.⁶ Greenstein finds that the presence of any exhibition of cancer uniformly results in a depression of the liver catalase.^{7, 8} Maver and Barrett describe substantial evidence for an immunological uniformity among malignant tumors.⁹ Greenstein reports an impressive degree of uniformity in enzyme concentration among malignant tissues, regardless of their means of induction, tissue of origin or species of origin.¹⁰ Others describe a uniformly low content of such aerobic catalytic systems as cyto-

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chrome, succinic, and d-amino acid oxidases, cytochrome-c, catalase and flavin.^{11, 12, 13, 14, 15, 16, 17}

Further phenomena of uniformity are observed in the elevated water and cholesterol content of malignant tumors as well as other primitive tissues.^{18, 19} The induction by a single steroid carcinogen, such as methylcholanthrene, of malignant exhibitions as diverse as leukemia and malignant melanoma, attests to a basically uniform etiology. The uniformity of various exhibitions of cancer in respiratory properties, lactic acid production, vitamin content, enzyme content, action on a given substrate, effect on liver catalase, cytochrome oxidase content, immunological properties, and many other characteristics is correlative to an uniformity of malignant tumors in the ability to metastasize, in their amenability to heterotransplantability,^{21, 22} and in their autonomy, invasiveness and erosiveness. Indeed, there is no known basic property unique to any single exhibition of cancer—the only variation being a morphological one partially conditioned by admixed benign or somatic components.

The degree in the uniformity of the factors described increases with the increasing malignancy with which the tumor is exhibited. Thus with an increasing degree of malignancy, all malignant exhibitions converge toward a common tissue type. For this reason the cells of the most malignant of all exhibitions of cancer should epitomize the properties of the malignant component in all other exhibitions of cancer. That this is the case, we shall observe in the pages that follow.

We have glanced briefly at data that are commonplace to cancer research. The logical consequences of these data have, however, seldom been examined. Since the phenomenon of cancer is truly an unitarian one, then, of logical necessity, the variations in the biological malignancy of different exhibitions of cancer must be a function of *the concentration of a cell of an intrinsically uniform malignancy.*

POSITION OF THE CANCER CELL IN THE LIFE-CYCLE

In accounting for the nature and origin of the single cell type comprising the constant malignant component in the varying morphological exhibitions of cancer, we find one of two alternatives open. The definitively malignant cell either has its normal counterpart in the life-cycle or the malignant cell is without a normal cellular counterpart and, therefore, arises as a spontaneous generation. Since spontaneous generation is an untenable postulate, the only alternative is that the malignant cell has its counterpart in the life-cycle. The question then arises whether this counterpart is a

relatively developed cell or the most primitive cell in the life-cycle. Since the primitivity of the cancer cell is a commonplace, in looking for its cellular counterpart in the life-cycle we turn to the most primitive cell in this cycle. This is the trophoblast cell. Then as a logical corollary of the unitarian thesis, we should find the trophoblast cell as the constant malignant component in all exhibitions of cancer: the malignancy of the cancer varying directly with its concentration of trophoblast cells and inversely with its concentration of somatic cells.

If the unitarian thesis is valid, then the most malignant exhibition of cancer possible should be comprised almost completely of *frank trophoblast cells*; and, in being so comprised, should epitomize the cellular and other phenomena shared by exhibitions of a lesser malignancy. The most highly malignant exhibitions of cancer known are the chorionepitheliomas comprised of *frank trophoblast cells*, cytologically, endocrinologically and otherwise indistinguishable from normal pregnancy trophoblast cells. If cancer is an unitarian phenomenon whose malignancy is a function of the concentration of trophoblast cells within a given tissue, then the greater the concentration of such cells within a tissue the higher the malignancy of the tissue and the more profound its cytological deviation from the cytology normal to the tissue. If the unitarian thesis is valid, then the single exception to this generalization would comprise the most malignant of all exhibitions of cancer: that involving the pathologic exhibition of the normally or "physiologically" malignant pregnancy trophoblast. It is, therefore, most significant that when pregnancy trophoblast is malignantly exhibited as primary uterine chorionepithelioma there is no *ascertainable cytological, endocrinological or other intrinsic change whatever from the normal trophoblast cell*. As Boyd has phrased it, "microscopically the chorionepithelioma is an exaggeration of the condition normally found in pregnancy."²³ All other tumors represent an attenuation of the condition of their normal tissue of origin.

PROPERTIES OF THE TROPHOBLAST CELL

But if cancer is, as an unitarian phenomenon, trophoblastic then we should expect to find occasionally in the male—where trophoblast never normally exists—at least some cases in which the failure in somatic resistance to the definitive malignant cell (trophoblast cell) is so complete that the trophoblast is frankly exhibited as such in the fiercely malignant testicular or primary extra-genital chorionepitheliomas.^{24, 25, 26, 27, 28} The chorionepitheliomas are unquestionably the most malignant tumors in either sex, and the degree of

their malignancy is routinely determined by measuring the gonadotrophin their trophoblast cells excrete.^{29, 30, 31}

If the trophoblast cell, presented outside the normal canalization or checks of pregnancy, is truly the cancer cell, then it must be impossible for the trophoblast cell or its hormone—"chorionic" gonadotrophin—ever to be found in the male or, aside from the canalization of normal pregnancy, in the female except in a malignant fashion. *Neither the trophoblast cell nor its hormone has ever been so found except as cancer.* And whenever the trophoblast cell or its hormone has been found in the male or the non-pregnant female, the associated malignancy is observed to vary directly with the urinary excretion of trophoblast cell-produced gonadotrophin.

Even a superficial examination of the trophoblast cell indicates that it possesses such properties of the cancer cell as invasiveness, erosiveness, autonomy, and ability to metastasize throughout the organs of the host.^{32, 33} Indeed, though normally canalized to physiological ends, the pregnancy trophoblast in carrying the conceptus from anatomically outside of the maternal host to implantation within the uterine wall must behave in a profoundly malignant fashion. No malignant cell invades any tissue any more rapidly and completely than the pregnancy trophoblast does the human uterus in the first few weeks of gestation.

If the trophoblast cell, then, is *intrinsically* malignant, this malignancy should become especially apparent when the trophoblast is removed from the normal extrinsic checks and controls surrounding it in its normal canalization of pregnancy. Maximov is among those who have observed normal pregnancy trophoblast in tissue culture *pari passu* non-trophoblast.³⁴ He describes as follows a tissue culture preparation of a normal rabbit embryo *plus* the contiguous trophoblast:

"From the very first moment of their formation *in vitro*, the trophoblastic elements, whose function under normal conditions is to destroy, resorb, and penetrate into the uterine mucosa, attack the growing embryonic tissues. They glide between the cells through the intercellular spaces, along blood vessels, gnaw large holes in epithelial sheets. . . . Wherever they appear they dissolve, destroy and resorb everything surrounding them. The picture sometimes bears a striking resemblance to *chorionepithelioma malignum*. As *in vitro* there is no maternal tissue, the destructive tendencies of the trophoblast are directed toward the next and only available—the embryonic tissue itself. This is rapidly destroyed and totally used up for the nutrition and growth of the trophoblast."

Maximov's description of the nutritive utilization by the trophoblast of somatic or embryonic tissue *in vitro* bears a striking parallelism to the following observation of Greenstein³⁵ on the nutritive behavior of the cancer cell:

"It is, indeed, astonishing that a tumor can thus attach itself to an organism already running downhill in negative nitrogen balance and subsequently grow at the host's further expense."

Parasitization is eloquently clear in the description given by Maximov and it is implicit in Greenstein's observation. Normal pregnancy trophoblast represents, of course, a parasitization of cells of one genetic constitution by those of another. If cancer is an unitarian and thereby a trophoblastic phenomenon, its parasitic behavior is very easy to understand.

Were pregnancy trophoblast *in vivo* or *in situ* to lack the humorally mediated checking influences that are lacking *in vitro*, then such tissue would expectedly behave as it does *in vitro* and be exhibited in the fiercely malignant fashion of primary uterine chorionepithelioma.

Rather than pause here to review in further detail the points of identity between the cancer cell and the trophoblast cell, of which the senior author in a review of over 17,000 papers has been able to catalogue 43, let it suffice to say that we have been unable to find a single point of dissimilarity between the cancer cell and the trophoblast cell. The points of identity, of course, are those shared exclusively by the cancer cell and the trophoblast cell and not shared by any somatic cell.

THE CELL OF ORIGIN AND THE MEANS OF ITS DIFFERENTIATION

If cancer is a truly unitarian phenomenon, then its cellular origin as well as its cellular nature are exemplified in the origin and nature of the most malignant exhibition of cancer—primary uterine chorionepithelioma.

Pregnancy trophoblast arises through the differentiation by meiosis of a diploid totipotent cell in response to *organizer stimuli* (afforded through the sex steroids). The meiosis of the diploid totipotent cell results in a haploid gametogenous cell whose only alternative to death is division (sexually or parthenogenetically induced) with the consequent production of trophoblast. The only cell from which the most primitive cell in the life-cycle, the trophoblast cell, can arise is the most undifferentiated or most potent

cell in the life-cycle: the diploid totipotent cell. It is this cell alone that is competent for meiosis. In fact, aside from the explanations of spontaneous generation, only two alternatives exist for the origin of the malignant cell. Like all other growth phenomena, it may arise as the result of the differentiation of an undifferentiated cell in response to organizer stimuli; alternatively, it may be ascribed to the ontogenetic "reversion" of normal cells to a primitive state. Even though the very notion of such reversion is a thermodynamic fantasy inadmissible by modern biology, if a normal cell could revert, the most primitive cell in the life-cycle toward which such reversion could occur is still the trophoblast cell. Hence, aside from the errors of spontaneous generation or cellular reversion, *only the phenomena of cellular differentiation are tenable in accounting for the origin of the cancer cell—though the stimulus to such differentiation may, of course, be diversely mediated.*

It is thus a simple embryological fact that the malignant component of the most malignant of all exhibitions of cancer—primary uterine chorionepithelioma—represents the unchecked growth of normal trophoblast that has arisen through the differentiation of a diploid totipotent cell, by reduction division, and the division of the consequent haploid gametogenous cell to produce trophoblast. We have seen the proof of this in the fiercely malignant behavior of rabbit trophoblast removed from the checking influence of the maternal host and placed in tissue culture. This trophoblast, of course, came into being through processes normal to the production of all trophoblast in normal gestation. This is true also of the trophoblast of primary uterine chorionepithelioma.

It is necessary that we emphasize here the fact that our description of the origin of *any* trophoblast cells is merely a recapitulation of commonplace, universally accepted embryological data. We must not permit terminology to obscure this fact. Let us add that it has been experimentally established that in mammals the haploid gametogenous cell in either the male or the female may be non-sexually activated into division with the consequent and inevitable production of trophoblast.

Because the trophoblast cell of primary testicular chorionepithelioma is indistinguishable from that of the normal pregnancy trophoblast cell^{36, 37, 38} or a trophoblast cell of primary uterine chorionepithelioma,^{39, 40} the general consensus in pathology that chorionepitheliomas arise from the division of a gametogenous cell (non-sexually activated), derived through the normal meiosis of a diploid totipotent cell, is biologically and logically sound. It is likewise generally recognized that *primary extra-genital* chorionepi-

theliomas occurring in both sexes represent trophoblast that shares a common cellular origin with all other trophoblast: an origin from an haploid gametogenous cell (through fertilization or non-sexually) that has arisen through the meiosis of a diploid totipotent cell. This principle is congruent with the axiom that cells which are alike arise from pre-existing cells that are alike.

INDEX OF MALIGNANCY

If cancer is an unitarian phenomenon in which all morphological exhibitions share, in varying degrees, the known malignant component of the chorionepitheliomas, then it follows (1) that the malignancy of a growth will vary directly with its concentration of trophoblast cells and inversely with its concentration of body or somatic cells; and (2) the trophoblast cells comprising a malignant lesion must possess the capacity for being morphologically masked or obscured by the tissue in which they primarily occur or to which they metastasize. Testicular chorionepitheliomas afford an interesting vantage point for the examination of these possibilities. In screening over 900 testicular cancers in the Army Institute of Pathology, Friedman and Moore (1946) reported, in part, as follows:⁴¹

"Nearly twice as many metastases which exhibited chorionepitheliomatous structures arose from primary tumors containing no chorionepithelioma as from pure chorionepitheliomas or neoplasms containing focal chorionepithelioma. While only 0.4 per cent of the primary testicular tumors were pure chorionepitheliomas and 6.4 per cent showed focal chorionepitheliomatous tissue, 27 per cent of all metastases which terminated fatally contained chorionepitheliomatous elements." (emphasis ours)

Thus, not only may the trophoblast, when frankly exhibited as such in the primary site, metastasize to be morphologically masked in the secondary site, but the primary trophoblast itself may be morphologically masked by the soma and be frankly exhibited only when metastases occur into tissues of relatively lower reactivity in which the trophoblast is not morphologically masked but is frankly exhibited as such. The masking of the trophoblast by the reactivity of the somatic cells is a measure of the resistance of the host: the degree to which such somatic resistance against the ectopic trophoblast fails determines the malignancy with which the trophoblast is exhibited. Thus, the greater the incidence of a chorionepithelio-

matous exhibition (trophoblast) in the metastases, the greater the degree of malignancy.

COMPETENT CELL AND ORGANIZER

The origin of every new cell is the result of the apposition of a competent cell and an organizer stimulus. All new cells arise as the result of cellular differentiation, which is a process by which a new cell type of a higher degree of individualization and a lower degree of developmental competence is produced. There are no exceptions to this generalization—not even the cancer cell. While a differentiated cell may become plastically deformed or necrobiotic, it can never form a new cell type through any means except the forward-moving course of cellular differentiation. Cellular reversion is a thermodynamic impossibility; it has never occurred and can never occur. Water will not run uphill—not even in cancer. The cancer cell is neither a deformed one nor a necrobiotic one. Its lethality resides in the very fact that intrinsically it is a normal cell—though its spatial and temporal relationship to the organism-as-a-whole is an abnormal one. The trophoblastic or unitarian thesis simply recognizes that: (1) the cancer cell is contained within the life-cycle and (2) that it is the most primitive cell in that life-cycle.

Though the diploid totipotent cells which give origin to trophoblast are known to be very abundant in the gonads, the question next arises as to their occurrence extra-genitally. Most modern pathologists^{42, 43, 44, 45, 46} recognize the existence of so-called ectopic germ cells (diploid totipotent cells) and Bounoure⁴⁷ has, in an extensive monograph, recently reviewed the conclusive observational and experimental evidence for the dispersion of such cells throughout the soma. Of course, embryologically, these cells are nothing more than totally undifferentiated cells that have not, as Arey phrased it,⁴⁸ participated in body building but have reserved their total potency or competency since the initial cleavage of the zygote. Cells of various degrees of undifferentiation exist within the soma as a reservoir from which tissue repair and regeneration occur. But only the totally undifferentiated cells of the soma are competent for meiosis; these cells are the diploid totipotent cells. Of course, all cells in the soma are diploid, but only those that are totally undifferentiated are totally potent or totipotent—hence competent for meiosis. That such cells exist as well as function in the soma is further proved by the occasional occurrence of primary extra-genital chorionepithelioma in the male in such regions of low tissue reactivity as the pineal gland^{49, 50} and the anterior

mediastinum.^{51, 52, 53, 54} The frankly exhibited trophoblast cells are correctly attributed to the only progenitor of trophoblast: a diploid totipotent cell that has undergone reduction division or meiosis to form a haploid gametogenous cell that has trophoblast formation as the only alternative to death.

Carcinogenesis is thus seen to be a phenomenon involving a spatially anomalous *differentiation* in response to organizer stimuli. (Primary uterine chorionepithelioma—as well as normal pregnancy trophoblast—while involving precisely the same differentiation in its origin, does not, of course, involve it anomalously.) The differentiation involves the phenomenon of meiosis with the consequent production of trophoblast, which, presented ectopically, is inevitably exhibited as cancer—the malignancy of which depends upon the extent to which such ectopic trophoblast is resisted. Thus in the unitarian thesis we see the malignant component in *all* exhibitions of cancer deriving from precisely the same cell type from which the chorionepitheliomas arise. We see all producing the same cell type—trophoblast. We see this cell doing ectopically precisely what it does in its normal canalization: eroding, infiltrating, and metastasizing.

"One of the most important problems in cancer research," Greenstein⁵⁵ points out, "is concerned with the question of why primary tumors metastasize." If cancer is trophoblastic, the problem of metastases is resolved: the normal pregnancy trophoblast is the *only* cell in the life-cycle that regularly metastasizes, doing so throughout the maternal host in the early months of pregnancy.^{56, 57}

The stimuli to malignant differentiation are exemplified in the sex steroids which induce the meiosis of diploid totipotent cells in their normal canalization. In view of the relatively specific organizer action of steroids, it is significant that practically all of the carcinogens are either steroids or, like diethylstilbestrol, possess the physiological properties of steroids. Though carcinogenesis may be mediated by highly diverse means, the ultimate common pathway involves the apposition of competent cell and organizer stimuli. The competent cell is always a totally undifferentiated cell (diploid totipotent cell) and the organizer stimulus ultimately involved appears to be a steroid compound.

Agents producing a chronic inflammation can also prove indirectly carcinogenic, since chronic inflammatory sites have a marked capacity for localizing or concentrating steroid sex hormones as well as other substances.⁵⁸ Certain chemicals may also prove indirectly carcinogenic through impairing the somatic detoxification mechanism for steroids.^{59, 60} That under special and very limited

circumstances viruses may also contribute to the common pathway by which malignant differentiation is accomplished in birds* and rodents is recognized. Virchow, however, pointed out 90 years ago that no stimulus can elicit from a tissue potencies not inherent within the tissue. The general consensus is that the role of the cancer virus is evocatory, eliciting from the organism an inherent potency; rather than creative, conferring *de novo* the cancer cell upon the organism.

ESTROGENS

Since the meiosis of normally canalized diploid totipotent cells is accomplished in both sexes through the organizer action of steroid sex hormones, a review of the formidable literature on the carcinogenic properties of estrogen correlated with the unitarian thesis would be most pertinent to a complete elucidation of the thesis. Space will not permit this, and it must suffice to say that the normal estrogens bear as crucially a basic relationship to the origin of malignant cells, under ordinary circumstances, as chorionepithelioma bears to their cellular identity.

VIRUSES AND SOMATIC MUTATION

Since the virus theory is subsumed under the unitarian thesis—as a specialized contributory means† of eliciting the malignant differentiation—the chief remaining theory is the somatic mutation hypothesis. This hypothesis explains nothing and is, in fact, little more than a circular definition: cancer is due to a change; a change is a mutation. This change occurs in the body or soma; therefore, cancer is due to a somatic mutation. On the other hand, the trophoblastic or unitarian thesis does embrace a very definite genetic “mutation.” This “mutation” is expressed as meiosis whereby, with the division of the consequent gametogenous cell, the ectopic trophoblast (cancer) cell presented to the soma is, through the necessity of meiosis, of a genetic composition unique from the soma; and, therefore, in the most literal genetic sense a neoplasm.

* The phylogenetic homologue of the trophoblast (extra-embryonic blastoderm) in birds is known to exhibit, under certain conditions, malignant properties: e.g., anidian formation⁶¹.

†Joseph Needham⁶² has cogently remarked: “It is an instructive exercise to read through the writings on the virus theory of cancer, substituting the words ‘active agent’ or ‘active extract’ for virus wherever it occurs. The results are illuminating.”

Even were one uncritically to accept the somatic mutation hypothesis⁶³ or the virus theory of cancer,⁶⁴ it would be necessary either to seek their resolution in the unitarian or trophoblastic thesis or to turn to a non-unitarian explanation. In which case it would be necessary, then, to postulate an indefinitely large variety of unknown cancer viruses or a similar variety of unknown somatic mutations to account for the origin of the cancer cell. But not even these would suffice since neither hypothesis could account for the fiercely malignant behavior of normal trophoblast *in vitro*—nor for the fact that this cell has never been found in a non-pregnant organism except as cancer.

MEIOSIS

We have observed that the extra-genital dispersion of diploid totipotent cells is a commonplace fact. We have specifically ascribed the origin of all morphological exhibitions of cancer to the meiosis of one or more such diploid totipotent cells with the consequent production of a gametogenous cell whose only alternative to death is division with the resulting production of trophoblast.

In the normal reproductive canalization the *only* way in which trophoblast can arise is through the meiosis of a diploid totipotent cell and the consequent division (non-sexually or by fertilization) of the resulting gametogenous cell to produce trophoblast. Therefore, one question alone remains here: can the same diploid totipotent cell in an extragenital site undergo meiosis to eventuate in trophoblast production?

As early as 1879 Arnold observed gametoid (meiotic) mitosis in malignant tissue. About twenty years later Farmer, Moore and Walker reported the occurrence of meiosis (heterotypic mitosis) at the border of malignant tumors.⁶⁵ In 1929 Evans and Swezy described in inflamed somatic tissue changes "strikingly similar to those of meiotic mitosis."⁶⁶ In 1936 Hearne observed meiotic changes in tissues cultured with methylcholanthrene⁶⁷ and Mendorff made similar observations in 1939 with estrone.⁶⁸

Diploid totipotent cells are dispersed throughout the soma. Meiosis occurs within the soma. Frank trophoblast cells occur within the soma—though inevitably in a malignant exhibition. They can arise only through the division of a gametogenous cell produced by the meiosis of a diploid totipotent cell. Frank trophoblast cells have never been found in the soma except as the most malignant exhibition of cancer—with the exception of pregnancy.

Indeed, the difficulty is no longer one of accounting for the

origin of the definitive malignant cell through the phenomena discussed, but rather one of seeking *any* explanation of how the meiosis of ectopic diploid totipotent cells, exposed to adequate organizer stimuli, could invariably be averted so as to preclude their normal differentiation to trophoblast, whose ectopic exhibition has never been known except in a malignant fashion. Frankly exhibited, such trophoblast comprises the most malignant exhibition of cancer possible, though when morphologically masked by the somatic response of the hostal cells the malignancy of such trophoblast is moderated.

UNITARIAN VS. NON-UNITARIAN THESIS

The body of experimentally established facts comprising modern oncology is formidable. It is not possible for any explicitly defined thesis to stand unless it is congruent with, or at least not contradictory to, such facts. Only the unitarian thesis finds such congruence. To the unitarian thesis in general and in particular to the preceding data outlined for it, it is especially instructive to apply Herbert Spencer's criterion of truth—the inconceivability of the opposite. The thesis opposite or alternative to the unitarian one is that each morphological exhibition of cancer represents a biologically distinctive phenomenon, each with a malignant component different from all others. This would mean literally hundreds of basically different types of cancer cells—each type being normally unrepresented in the life-cycle; therefore, each being spontaneously created. Not only would it become necessary to postulate the existence of hundreds of distinct species of cancer cells, but also a postulate of an almost infinite number of subspecies of each type of cancer cell would be required to account for the varying degrees of malignancy exhibited by a given malignant lesion in the course of its evolution. Since a single chemical carcinogen can evoke practically any malignant exhibition, then it would become necessary—according to any non-unitarian concept—to conclude that causes which are alike produce effects that are unlike. On the same basis, the occurrence of the frankly exhibited trophoblast cells of extra-genital chorioneopithelioma in the male (identical with those of the primary uterine form) would necessitate the unbiological conclusion that cells which are alike arise from cells that are unlike. The logical negation of *any* non-unitarian hypothesis is further apparent in the experimentally defined uniformity of cancer cells in every one of over twenty factors studied to date.

In contrast to the alternative non-unitarian hypothesis, the uni-

tarian thesis holds that the malignant component in all exhibitions of cancer is the same; that this component is not spontaneously created but represents the most primitive cell in the life-cycle; that this cell arises not through "reversion" but through differentiation; that the varying morphological exhibitions are simply conditioned by the nature and resistance of the tissue in which the ectopic trophoblast finds itself; and that the malignancy of the exhibition is, roughly, expressed in the degree of deformation of the somatic tissue by the ectopic trophoblast—and that this is reflected in the morphology from which histological diagnoses derive.

The unitarian thesis and the trophoblastic thesis are of logical necessity synonymous: the most malignant exhibition of cancer (chorionepithelioma) comprises cells intrinsically identical with pregnancy trophoblast cells.* Then, if cancer is an unitarian phenomenon, the malignant component of the varying morphological types must be trophoblastic; for, two quantities equal to a third are equal to each other.

Finally, were we to set aside all else evidential of the unitarian or trophoblastic nature of cancer, and scrutinize but a single datum, we should find that neither experimental fact nor scientific reasoning can offer any alternative to the trophoblastic nature of cancer in explanation. This one datum is the fact that many authors over the past half-century have described frank trophoblast (chorionepithelioma) metastasizing from a primary site to appear at the secondary site in an adenocarcinomatous or other exhibition.^{69, 70, 71} And the converse has frequently been seen.⁷² Moreover, frankly exhibited trophoblast (chorionepithelioma) often has been described as merging by imperceptible degrees into an adenocarcinomatous or sarcomatous exhibition. In their comprehensive monograph on chorionepithelioma, Park and Lees (1950) write:

"There is no doubt that in many instances of testicular chorionepithelioma, certainly in several of our sections, characteristic trophoblast merges imperceptibly with areas of undifferentiated tissue whose hostal origin would never be questioned."⁷³

THE TROPHOBLAST AND THE PANCREAS

John Beard, a lecturer in embryology at the University of Edinburgh, first published on the trophoblastic thesis of cancer in June,

*The malignant exhibition of the trophoblast of the placenta is the expression of a lack of *extrinsic* growth restraints against the trophoblast; this fact was demonstrated in the tissue culture of normal rabbit trophoblast.

1902.⁷⁴ By February, 1905 he reported, on embryological grounds, the antithesis of the pancreatic enzymes to the trophoblast cell;⁷⁵ and, a few years later he specifically pointed out that the cancer or trophoblast cell protected itself against pancreatic enzymes through the production of specific antitryptic substances.⁷⁶ The occurrence of tryptic inhibitors in cancer sera has, during the past forty years, been described by at least fifteen different workers,⁷⁷⁻⁹² though not within the context of the trophoblastic thesis.

In 1947 Krebs, Krebs and Gurchot first pointed out the specific antithesis of chymotrypsin to the malignant (or trophoblast) cell.⁹³ In 1948 Clark, Cliffton and Newton further confirmed the specific antitryptic antithesis of the cancer cell and offered evidence for the diagnostic and prognostic utilization of the phenomenon. In 1949 West and Hilliard, in the study of the sera of over 3,000 cancer patients, reported the specific antithesis of the malignant cell to chymotrypsin by showing that 15 grams of crystalline chymotrypsin would be necessary—in a single dose—to neutralize all of the *average excess of chymotrypsin inhibitor* in the serum of the advanced cancer patient. The latter workers proposed the utilization of the specific antichymotryptic titer of the serum for prognostic but not necessarily diagnostic purpose.^{88, 91}

It is noteworthy that West and Hilliard, as well as others, have described a quantitative relationship between the concentration of cancer cells and the titer of specific chymotrypsin inhibitor. This titer was observed to fall after the surgical removal of the malignant tumor and to rise linearly with its recurrence. Thus the data on the antitryptic properties of cancer sera are not only proof of the antithesis between the cancer cell and the pancreatic enzymes, but are further evidential of the unitarian—and thereby trophoblastic—nature of cancer.

Since the malignant cell is not spontaneously created but has its normal counterpart in the most primitive cell of the life-cycle, each organism in the span of its own gestation destroys the cellular counterpart of cancer. This destruction is accomplished through the pancreatic enzymes, notably chymotrypsin and amylase.

When the mammalian organism totally fails in this, the pregnancy trophoblast overgrows as chorionepithelioma.⁹⁴ A partial failure is reflected as a toxemic pregnancy,⁹⁵ and/or a hydatidiform mole accompanied by an abnormally high excretion of chorionic (trophoblastic) gonadotrophin. For this reason hydatidiform moles are most frequently associated with toxemic pregnancies, while the risk of sequent chorionepithelioma is 2,000 to 4,000 times greater after hydatidiform mole than after normal pregnancy.⁹⁶ The reason for "the much higher curability rate of choriocarcin-

noma preceded by hydatidiform mole," as reported by Park and Lees,⁹⁶ is that the precedent hydatidiform mole represented at least a partially successful antithesis on the part of the maternal host to the trophoblast.

The reason why primary uterine chorionepithelioma can within a few weeks arise and kill the patient is that this most malignant tumor simply represents a *hyperplasia* of normal trophoblast cells freed from their extrinsic restraint—just as the *in vitro* culture of the rabbit trophoblast freed from the maternal environment yields a fiercely malignant exhibition.

It is well established^{*} (1) that pregnant diabetics exhibit a greatly increased incidence of the pregnancy toxemias; (2) that the severity of such toxemias varies directly with the overgrowth of cellular trophoblast as reflected in the abnormally elevated excretion of chorionic gonadotrophin; (3) that the phenomenon involves a non-insulin deficiency of the pancreas gland; (4) that the predisposition to pregnancy toxemias is noted as early as five years^{97, 99} prior to the clinical onset of diabetes; (5) that the administration of steroid sex hormones in such pregnancy toxemias frequently ameliorates the condition; and (6) that this amelioration is reflected in a proportionate depression in the urinary excretion of chorionic gonadotrophin.

Since such steroid sex hormones as estrogen depress the proliferation of cellular trophoblast both in normal and toxemic pregnancies, as reflected in a depression in the urinary excretion of chorionic (cytotrophoblastic) gonadotrophin, it is significant that Kullander (1948) found in primary uterine chorionepithelioma that the administration of stilbestrol resulted in a clinical improvement that paralleled the decline in the urinary excretion of chorionic gonadotrophin.¹⁰⁰ Though Kullander did not cure his patients, so long as stilbestrol controlled the excretion of chorionic gonadotrophin, they improved.

It is a commonplace observation that the administration of estrogen or testosterone during pregnancy will often depress the production of chorionic gonadotrophin sufficiently to cause the Aschheim-Zondek test or its Friedman modification to become negative.

In listing the criteria of malignancy, Oberling and Woglom write: ". . . Above all is the impudent independence called autonomy."¹⁰¹ Certainly, no other property is more characteristic of the cancer cell than autonomy; yet in the most malignant exhibition

*The complete bibliography for these data is given in Krebs & Bartlett's (1949) monograph on "The Pregnancy Toxemias, the Role of the Trophoblast and the Pancreas."¹²²

of cancer possible we find the trophoblast cells showing the same susceptibility to the checking influence of sex steroids as is found for the normal pregnancy trophoblast.

If cancer is trophoblastic, and as such an unitarian phenomenon, it would seem that the steroidal sex hormones should suppress the growth not only of pregnancy trophoblast and chorioneopithelioma but all other exhibitions of cancer as well. That this would be the case were sufficient localization of the steroidal sex hormones possible at all malignant sites is shown in the fact that these hormones do act to suppress the growth of mammary cancer, prostatic cancer, and their metastases involving the skeletal system. Morphologically, the difference between a primary mammary cancer and a prostatic one is much less pronounced than the difference between either and a primary chorioneopithelioma.

The placenta, the prostate, and the mammary gland are notably capable of the selective localization of steroids; hence, trophoblast in any of these areas will show a like response to the injection of steroidal sex hormones. In the case of prostatic and mammary growths the use of the physiologically antagonistic steroid is rational, since such causes the somatic elements in the growth to atrophy. That the palliative effect is dependent upon the ability of the *somatic* elements in the tumor to localize the steroids is shown in the fact that the skeletal metastases from the prostate as well as from the mammary gland are responsive specifically to estrogen and testosterone, respectively. Yet this amenability is lost as, with increasing malignancy, the original somatic elements in the skeletal metastases are lost. That such a loss is not directly due to the increasing malignancy but indirectly to the loss of the specific somatic cells responsible for the localization of the steroids is indicated by the fact that in the placenta, while the localizing somatic elements remain, the growth of the vastly more malignant chorioneopitheliomatous exhibition is checked.

Thus we find the unitarian principle of cancer implicit in the sex hormone therapy of cancer, as in *all* other useful forms of cancer therapy. Moreover, in the unitarian principle the use of steroidal sex hormones in cancer finds its first rationale.

Since a non-insulin pancreatic deficiency has been identified with the overgrowth of pregnancy trophoblast, which overgrowth has been shown amenable to steroidal sex hormones, two questions arise: (1) what is the nature of the deficient pancreatic factor, and (2) is the deficiency of this factor associated with the overgrowth of *all* trophoblast? About half a century ago John Beard¹⁰²⁻¹¹⁹ found a concomitance between the commencing function of the fetal pancreas, as indicated by the appearance of zymogen gran-

ules in the gland, and the precipitate degeneration of the trophoblast or its phylogenetic homologue. Broad comparative studies confirmed his thesis that, in the span of normal gestation, the pancreatic enzymes are responsible for checking the growth and ultimately destroying the gestational trophoblast or its homologue. In fact, Beard's studies were so carefully performed that he was able to state half a century ago that in the 56th day in the span of human gestation the cellular trophoblast undergoes a sudden degeneration. Some 30 years after this work, the trophoblast cell-produced chorionic gonadotrophin was discovered, and only recently has the quantitative technic for the estimation of chorionic gonadotrophin been sufficiently perfected to show that a composite¹⁰² excretion curve for chorionic gonadotrophin made through the span of human gestation coincides¹²⁰ precisely with the curve predicted half a century ago by John Beard.

If the urinary excretion of chorionic gonadotrophin persists at the original level after the 56th to 70th day in the span of human gestation, the process is inevitably exhibited as chorionepithelioma. In fact, if the abnormal elevation of chorionic gonadotrophin found in pancreatic dysfunction in pregnancy exceeds a certain level, again the process is exhibited as chorionepithelioma.

In view of the antithesis of the pancreatic proteases to the trophoblast cell, it is clear why both pregnancy and cancer are associated with high titers of trypsin and chymotrypsin inhibitors: antithesis is a two-way street, so to speak.

If the pancreatic enzymes are antithetic to the cancer cell, if they resist the cancer cell as the cancer cell is known to resist them (through the specific antitryptic inhibitors) why does cancer of the pancreas gland occur? Why is it that cancer is not only primary in this gland but that this gland itself may be subject to secondary growths through metastases or direct invasion?

The pancreatic proteases exist in the pancreas in the form of their *inactive* zymogens. These are not converted into the corresponding active enzymes until they are acted upon by the kinases of the blood or, especially, by those of the small intestine. In view of this, one may ask why the small intestine, then, is not practically immune to cancer. Woglom answers this question well in his commentary in an abstract of a paper by Raab:^{120, 122, 123}

"One of the most striking features about the pathology of malignant disease is the almost complete absence of carcinoma in the duodenum and its increasing frequency throughout the gastro-intestinal tract in direct proportion to the distance from this exempt segment."

It is noteworthy that the small intestine is not only practically immune to primary tumors but also to metastases. A fulminating malignant growth may exist in the pyloric end of the stomach a few millimeters from the immune small intestine, but, as William Boyd points out, "The duodenum is never invaded, the tumor stopping short at the pylorus. Spread to neighboring organs usually involves the liver or the pancreas."¹²⁴ The incidence of malignancy is, of course, high immediately distal to the ileocecal valve.

The pancreatic enzymes not only normally occur in the active state in the blood stream, which possesses an optimum pH for their action, but the clinical determination of serum amylase and trypsin are standard procedures, especially in pancreatic diseases.

THE PANCREAS AND CARCINOGENESIS

The fact that pregnancy occurs in the presence of a normal concentration of pancreatic enzymes indicates that trophoblast can exist for a while under such conditions. It must be remembered, however, that such trophoblast is: (1) held in check until the 56th day of gestation and almost completely destroyed shortly thereafter (with the commencing function of the fetal pancreas) and (2) that implantation occurs *after* the trophoblast has had about a four-day period of growth anatomically exterior to the host.

The trophoblast carries with it its own antitryptic enzymes against the pancreatic proteases. As we have seen, carcinogenesis involves ectopically precisely the same basic mechanisms involved in the production of canalized trophoblast. The prolonged exposure of a tissue to carcinogens results in a prolonged depression in its respiratory mechanisms.¹²⁵ This may result in the appearance and persistence of ectopic trophoblast in the exposed tissue. The trophoblast or cancer cell is autonomous of the hostal respiratory system and is obligatively anaerobic, undergoing aerobic glycolysis even in the presence of a free oxygen supply.¹²⁶ The trophoblastic thesis explains the long-known identity of trophoblast cell metabolism with that of the cancer cell:^{127, 128, 129} an obligative anaerobic system is obviously a necessity in a primitive parasitic cell like the trophoblast (or cancer) cell.

When cancer is elicited experimentally from a normal laboratory animal, the lesion usually does not metastasize, but attains a large size and is almost completely somatic. Herein reside the scientific limitations of artificially induced or transplanted animal tumors in the scientific study of chemotherapeutic agents. Such tumors are practically benign in a biological sense. Because the pregnancy trophoblast regularly and normally metastasizes in the early phase

of gestation, we must expect metastases ultimately in any "full blown" cancer.

While a low-grade malignant growth (primarily somatic tumefaction) can be induced ultimately by sufficient carcinogenic stimuli in the presence of normal pancreatic function, a highly malignant exhibition is invariably accompanied by at least a relative pancreatic insufficiency implicit in the correspondingly high serum titer of antitryptic and antichymotryptic enzymes.

That the induction of the ectopic trophoblast is usually accomplished against great difficulty—regardless of pancreatic adequacy—is indicated in the fact that non-chorione epitheliomatous exhibitions in man usually have a latent period of years, while a chorione epithelioma in pregnancy may arise from the preexisting trophoblast and destroy the host within a few weeks.

The extent to which the soma resists malignant involution is reflected in the fact that only two cellular differentiations—meiosis of the diploid totipotent cell and subsequent division of the resultant gametogenous cell—divide the malignant cell from the benign one. This explains the all-or-none suddenness classic to the malignant change—and the absence of true transitional cells.

CANCER A COMPOSITE TISSUE

The malignant lesion is a composite tissue comprising (1) trophoblast plus (2) somatic elements. The malignancy of a lesion varies directly with its concentration of trophoblast and inversely with its concentration of somatic elements. The normal placenta, too, represents a composite tissue; for, here the trophoblast cell finds its normal canalization in the life-cycle. Just as the malignancy of a placenta, in a chorione epitheliomatous exhibition, varies directly with the concentration of trophoblast cells, so in the ectopic presentation of trophoblast that comprises cancer the malignancy of the lesion varies with its concentration of trophoblast. The only fundamental difference is that in the latter the trophoblast cells are morphologically masked by the resisting soma—except in the most malignant of extra-genital tumors: chorione epithelioma.

A tissue can be malignant only by being a composite one. Malignancy is an antithetic relationship between cells and finds being by virtue of a thetic benignity. In its simplest terms, then, a malignant tumor comprises somatic tumefaction plus a malignant component. It is for this reason that the greatest tumefaction is usually associated with the least malignant exhibitions and the least tumefaction often with the most malignant exhibitions. Since

trophoblast normally metastasizes, tumors of the highest malignancy and lowest tumefaction tend to be the most metastatic. Thus the increase or decrease in the malignancy of a given tumor is not the result of a continuing spontaneous generation of an infinite variety of cancer cells, *but merely the expression of the increase or decrease in the concentration of a constant malignant component.* As the antithesis of this component determines the malignancy of the lesion so that of the soma determines its benignancy.

LEUKEMIA

In the leukemias the constant malignant component (trophoblast) is present in the lymphopoietic or myelopoietic tissues. The reaction of such tissues to the malignant component results in the proliferation of *somatic* white blood cells of varying degrees of maturity. This is the counterpart of tumefaction in the sessile tumor. Thus the unitarian or trophoblastic thesis, different from the non-unitarian concept, finds no contradiction in the fact that often the most malignant phase of the leukemic process—the so-called aleukemic leukemia—actually involves a leukopenia. This phase is the most malignant because the somatic cells (leukopoietic tissue) have lost their ability to resist through virtue of the destruction of the leukopoietic tissue by ectopic trophoblast. For this reason the aleukemic or leukopenic stage is often terminal to a preceding highly leukemic or leukocytic phase.

TROPHOBLASTIC HORMONES

The routine utilization of the trophoblastic hormone, chorionic gonadotrophin, is, of course, a clinical commonplace as a means of diagnosis and as an index to therapeutic response in the case of the most malignant exhibitions of cancer—the chorionepitheliomas and certain other exhibitions of cancer. The excretion of this hormone varies directly with the malignancy of the tumor, which, in turn, varies directly with the concentration of trophoblast cells.

In 1944 Roffo¹³⁴ reported a similar gonadotrophin in all of 1,000 cancer patients examined, and none in the blood or urine of the control series—with the exception of pregnancy, of course. In 1946 Krebs and Gurchot¹³⁵ reported the identification of Roffo's gonadotrophin as trophoblastic. In 1947 Beard, Halperin and Liebert published a confirmation of the prior papers and suggested a practical utilization of the phenomenon.¹³⁶ Prior to these studies numerous scattered reports of chorionic gonadotrophin in cancer serum and urine appeared in the literature but without the con-

text of any unified theory. Zondek reported the hormone in the urine of 82 per cent of females afflicted with cancers of the genital organs and in 36 per cent of female patients suffering from extra-genital tumors.^{137, 138} Five years later Zondek was able to duplicate and extend his original findings,¹³⁹ which had been confirmed by others.^{140, 141, 142}

It is necessary to emphasize that the original work of Zondek as well as other workers was done on the erroneous assumption that the hormone was produced by the anterior pituitary gland. Even after tissue culture studies had proved the trophoblast-cell-origin of the hormone, its occasional identification in cancer urines, through the use of the Aschheim-Zondek or Friedman tests, was usually dismissed as an inexplicable datum of an inexplicable disease. Only within the context of the unitarian or trophoblastic thesis was sufficient theoretical justification found to concentrate and selectively extract the urines of the less malignant exhibitions of cancer specifically for the same hormones (chorionic gonadotrophin and syncytial steroids) always found by ordinary technics in the most malignant exhibitions.

Thus to the already established uniformities for 20 or more known factors among the various exhibitions of cancer, we now find an hormone uniformity (not only evidential of the unitarian thesis but of the specific trophoblastic nature of cancer as well) in the trophoblast cell-produced hormones. *Like all other uniformities found in the malignant lesion*, that for the trophoblastic hormones becomes increasingly apparent with the malignancy of the growth, so that frank chorione epitheliomas are found excreting as many as one million International Units of chorionic gonadotrophin every 24 hours, while the much less malignant exhibitions with no frank trophoblast cells excrete 50 or fewer units of the trophoblastic hormone.

DIAGNOSTIC IMPLICATIONS

There are only two fundamental kinds of cancer tests: (1) the indirect tests concerned with the detection of a substance produced by the soma as the result of the presence of cancer cells; and (2) the direct tests concerned with the detection of a substance produced by the cancer cells themselves. Though the incidence of a specific somatic change may bear a high correlation with the presence of an uniform stimulus, the correlation can never be a truly specific one, since obviously no somatic reaction is so specifically reserved for the presence of cancer or trophoblast cells that it can not be falsely elicited by other stimuli.

The limitations of the indirect tests have been well demonstrated in practice. The only reliable and generally accepted serum or urine tests for cancer are the direct ones, such as the Aschheim-Zondek test and its numerous modifications. Just as hundreds of indirect tests have been tried and discarded for pregnancy diagnosis, so have hundreds of indirect tests for cancer been tried and then discarded. The only tests for either pregnancy or cancer that have survived are those *direct* tests depending upon the identification of a substance unique to cancer and pregnancy: the hormone of the trophoblast cell. Since cancer is trophoblastic, its most malignant exhibition—chorionepithelioma—is highly amenable to the direct test. In fact, the possibility of either an indirect or direct general diagnostic test for cancer depends upon cancer being an unitarian phenomenon.

The efficient clinical implementation of the trophoblastic or unitarian thesis depends upon the development of a simple, reliable and highly accurate quantitative test for the specific products of the trophoblast cell.

While we have identified the presence of chorionic gonadotrophin in the urines of patients with all exhibitions of cancer, we have found the technological evolution of a quantitatively precise chorionic gonadotrophin test difficult for the less malignant exhibitions of cancer. When we consider that a chorionepitheliomatous exhibition of cancer in the male may yield over 1,000,000 I. U. of chorionic gonadotrophin while metastatic testicular cancers of a much lower malignancy—though biologically still more malignant than most extragenital growths—may yield fewer than 50 I. U. for a like volume of urine, then the physical difficulties in the case of most of the extragenital tumors of still lower malignancy is obvious.

From the urines of patients with the common exhibitions of cancer, the authors have obtained highly active preparations of chorionic gonadotrophin, and are now engaged in the crystallization of chorionic gonadotrophin, by the method of Claeson, Höglberg and Westman (1948),¹⁴³ from pooled urines of various exhibitions of cancer. It is recognized that the specific steroid hormones of the syncytial trophoblast also comprise a most important avenue to the development of a satisfactory diagnostic technic. However, these steroid hormones have not been studied as intensely as chorionic gonadotrophin which is now characterized as a glucoprotein containing 18 per cent acetylglucosaminidigalactose polysaccharide.

Several cancer tests relying on the detection of trophoblastic

hormones are now under study for the purpose of achieving a sufficiently practical quantitative test for general use.

CLINICAL IMPLICATIONS

As a composite tissue, cancer in its somatic component represents many diseases; in its constant malignant component, one disease; and, in its totality, a local manifestation of a general disease. Since the perspective of the clinician is necessarily anthropomorphic, he sees cancer primarily in its somatic phase as a series of many diseases. On the other hand, as Oberling and Woglog have so aptly phrased it, "To the experimentalist cancer is one disease and one disease only."

Both clinician and experimentalist are generally agreed that the somatic or anatomical changes produced by the malignant process are largely irreversible. Surgical extirpation or the primarily non-selective cautery of radiant energy may destroy the composite tissue of a primary tumor. But the vague hope for an agent that will cause the "reversion" of an organized malignant tumor to normal tissue is scientifically indefensible. Aside from the physical destruction of the tumor itself, one primary factor can contribute to the amelioration of the effect of the tumor on the host. This is the growth inhibition or destruction of the constant malignant component of the tumor. Selective ablation of the malignant component will not alter the already existing somatic dysplasia nor histologically change the architectonics of the tumor, except in highly malignant anaplastic exhibitions. Here the histological as well as the gross changes take an expected course: an histological increase in connective tissue elements with a palpable increase in fibrosity.

In the advanced and well organized lesion, the possible changes are not, as a rule, dramatic. Were the malignant component ablated, the somatic component would tend to persist largely unchanged, or even show a slight increase in benign tumefaction. Since none of the cells in a malignant tumor is *per se* a "diseased" or pathological cell, but rather a cell normal to the life-cycle, cancer does not itself produce any "toxic effects." Its lethality is eminently a physical matter involving the normal behavior of normal trophoblast in a spatially abnormal relationship.

Above all, cancer is a natural phenomenon ultimately involving the soma in irreversible changes. To question the results expected from the selective ablation of the constant malignant component in a malignant lesion would be to suggest that, aside from actual tumor destruction, no malignant tumor has ever spontaneously regressed, that no highly anaplastic cancer has ever spontaneously

gone into a less malignant scirrhous exhibition, or that no patient has ever survived for five years or more after exhibiting an inoperable and highly malignant lesion. It is not necessary to review here an impressive literature on spontaneous regression. Much more important to a sound comprehension of the clinical implications of the trophoblastic or unitarian thesis are the thousands of cases of cancer in which the host is able to resist and to live with the cancer cells for years.

What are the factors—cells, tissues, organs, and their secretions—contributing to such resistance? What causes trophoblast in the pregnant diabetic to overgrow, despite a normal insulin supplement? Why do the specific inhibitors to pancreatic chymotrypsin and trypsin rise with the increasing malignancy of a growth and decline following its amelioration? Why is the small intestine practically immune not only to primary tumors, but to direct invasion and metastases as well? Why does the growth of the invasive, erosive and metastatic trophoblast of normal gestation cease and degeneration commence concomitant with the commencing function of the fetal pancreas gland? Why does the urinary excretion of chorionic gonadotrophin fall concomitantly with the degeneration of the trophoblast? After more than 99 per cent of the trophoblast has been removed from the placenta, why does its size remain unaffected though its invasive and erosive properties are entirely lost? Why are pregnancy trophoblast cells often indistinguishable histologically from the somatic cells in the uterine wall of the pregnant host? Why is it that the removal of normal pregnancy trophoblast to tissue culture will result in a fiercely malignant exhibition of such trophoblast toward *all* non-trophoblast cells?*

Any attempt to implement clinically the trophoblastic or unitarian thesis should be made in the light of the answers to these questions.

RADIATION

Were malignant cells actually selectively susceptible to radiation, the most malignant exhibitions of cancer would be the most amenable to therapy, since they would, then, contain the highest concentration of radio-sensitive cells. Chorionepithelioma and malignant melanoma represent two of the most malignant exhibitions

*The answers to these questions reflect the cogency of Oberling's prediction: "Some day, perhaps, it will turn out to be one of the ironies of nature that cancer, responsible for so many deaths, should be so indissolubly connected with life."¹¹⁸

of cancer, yet they are radio-resistant. Glioblastoma multiforme and neurogenic sarcoma are also examples of highly malignant exhibitions of cancer that are radio-resistant.

We may generalize that the malignant component of a tumor is *slightly* less radio-resistant than the somatic connective tissue stroma but considerably more radio-resistant than the somatic parenchyma. This is why radiation often results in an increase in tumor fibrosis, which would be an excellent sign were this achieved at the cost of the radio-resistant malignant component (trophoblast) rather than at the cost of the somatic parenchyma. The so-called radio-sensitivity of a tumor is determined primarily by the radio-sensitivity of the somatic cells in which the constant malignant component happens to reside—not by the uniformly radio-resistant constant malignant component: the ectopic trophoblast.

RADIO-ACTIVE ELEMENTS

The most commonly used radio-active element is that of iodine in the therapy of cancer of the thyroid. Rhoads^{144, 145} describes the limitations of this therapy as follows:

"The more malignant and destructive forms tend to pick up (radio-active iodine) to a lesser and lesser degree as the invasiveness increases."

With an increase in the malignancy of the exhibition, there is necessarily an increase in the concentration of the definitively malignant cells (trophoblast) and a consequent decrease in somatic thyroid cells which are the only cells involved in the selective uptake of radio-active iodine. The decrease in tumefaction as a result of the uptake of radio-active iodine is an expression of the loss of functional somatic cells. This fact is further demonstrated in the successful use of this technic in toxic goiter.

SURGERY

The lower the concentration of trophoblast cells in a malignant lesion, the more amenable the lesion is to successful surgery. For this reason highly malignant growths like chorionepithelioma are generally inoperable.

PANCREATIC ENZYME THERAPY

The palliative use of the crystalline pancreatic enzymes in ad-

vanced human cancer rests *entirely* upon the validity of the unitarian or trophoblastic thesis of cancer.

CONCLUSION

Our own studies, too, appear to confirm the unitarian or trophoblastic thesis of cancer. The independently proved uniformities—which increase in degree of uniformity with the malignancy of the growth—of malignant lesions in the concentration of eight water-soluble vitamins; in vitamin C content; in water content; in cytochrome-c; in effect on liver catalase of the host; in Warburg's criteria of glycolysis; in lactic acid formation; in sugar content; in the respiratory response to added substrates; in a common means of induction; in antichymotryptic factors; in autonomy, invasiveness and erosiveness; in ability to metastasize; in amenability to universal therapeutic measures; in the general anticarcinogenic effect of caloric restriction on the incidence of mammary tumors and leukemia alike in experimental animals; in heterotransplantability; in loss of specialized function as malignancy increases (in all tumors except chorionepithelioma); in departure from the histology of the site of origin (except in primary uterine chorionepitheliomas);* in numerous enzymes—all these uniformities, indeed, exclude any but an unitarian nature of cancer. Then as we examine the most malignant exhibition of cancer possible—chorionepithelioma—to find it comprised of trophoblast cells indistinguishable cytologically, endocrinologically or otherwise from those of normal pregnancy trophoblast, the fact becomes impelling that if cancer is, indeed, an unitarian phenomenon, all of its properties must be exemplified in these most primitive of all cells in the life-cycle, the trophoblast cells. These cells in their normal canalization of pregnancy (as well as *in vitro*) exhibit *every known property of malignant cells*—though normally directed in pregnancy toward the physiological exploitation of the truly malignant process implicit in

*These are, indeed, instances in which the exception *proves* the rule; for, were cancer not trophoblastic, its most malignant exhibition—chorionepithelioma—would then show the greatest loss of function and the greatest deviation from the histology of the site of origin, instead of actually showing an accentuation in the normal function of trophoblast, as it does. Yet were one to attempt to ascribe to the malignant exhibition of trophoblast some *intrinsic* but subtle change from that of the non-malignantly exhibited trophoblast, such an attempt would be rendered nugatory by the fact that the most malignant exhibition of cancer possible in the male—chorionepithelioma—comprises trophoblast cells indistinguishable from those of pregnancy or chorionepithelioma in the female; yet, in the male chorionepithelioma represents the widest possible deviation in histology and function from the site of origin. The latter fact corroborates the proof of a rule previously proved by its exception.

the embedding of the tissue of the conceptus into that of the mother.

Then, were all else evidential of the unitarian or trophoblastic nature of cancer set aside, and were there left for scrutiny but the single fact that primary exhibitions of trophoblast (chorionepithelioma) are not infrequently seen that metastasize to an adenocarcinomatous or sarcomatous exhibition, and vice versa, then reason would admit of only one explanation: the trophoblastic or unitarian fact of cancer.

Were the cellular counterpart of cancer not an inextricable component of the life-cycle, represented in the most primitive cell of that cycle, the processes of natural selection themselves would have precluded the survival of the spontaneously generated cells that any alternative to the trophoblastic fact of cancer necessitates.

The unitarian thesis is not a dogma inflexibly held by its proponents; it is merely the only explanation that finds *total* congruence with *all* established facts on cancer. While the unitarian or trophoblastic thesis seemingly admits of no alternative, it warrants the most corrosive scrutiny. For cancer either is or is not an unitarian phenomenon, and thereby it is either trophoblastic or not trophoblastic in nature. The definitive cancer cell is either the most primitive cell in the life-cycle or it is not the most primitive. It is either the result of the *differentiation* or meiosis (however spatially or temporally anomalous) of a cell or it is not the result of cellular differentiation. It either has its normal cellular counterpart in the life-cycle, and thus is the result of cellular differentiation; or it has no cellular counterpart in the life-cycle, does not arise through cellular differentiation, and, therefore, is spontaneously created. The diploid totipotent cells within the soma, like their normally canalized daughter cells, can either undergo meiosis and subsequent trophoblast production, in response to sufficient organizer stimuli, or they can not. The occurrence of frank trophoblast cells within the soma (*invariably* as the most malignant exhibition of cancer) is either the result of the meiosis of a diploid totipotent cell or it is not; and, therefore, is the result of a spontaneous generation. The trophoblast or the cancer cell either produces specific inhibitors to pancreatic chymotrypsin and trypsin, or it does not (and the twenty or so independent workers who have so reported are all in error). A malignant tumor is either a composite tissue or it is not a composite tissue. The malignancy of a tumor is either determined by the concentration of a constant malignant component; or it is not so determined and depends, therefore, upon the successive spontaneous generation of a series of specific cells to account for the increasing malignant evolution of the tumor.

The trophoblastic or unitarian thesis holds the affirmative of all these propositions. It holds that *any* alternative to them will result in a *reductio ad absurdum*. The unitarian thesis recognizes the need for an orderly defined common ground of theory upon which all workers in cancer may at least meet, if not agree. It holds as reasonable the thesis that the more tenable of *two distinctly opposed hypotheses* should be given the greater credence in determining the direction of future research. It holds that in the intensive study of the peculiar metabolism of trophoblast both in pure cultures and *in vivo*, with the goal of the selective lysis of the trophoblast cell or the occlusion of its metabolism, the cancer problem may find practical resolution. It holds that the cancer problem need not offer amnesty to unbridled empiricism and negation to the most basic tenets of the rational process.

Above all else, the trophoblastic or unitarian thesis urges that the alternative non-trophoblastic or non-unitarian thesis, which is at present overwhelmingly the dominant hypothesis, be scrutinized in the light of whatever experimental evidence might exist in its support.* Indeed, the evaluation of *any* alternative to the trophoblastic or unitarian thesis—within the context of experimental facts and scientific logic—by those who find the trophoblastic or unitarian thesis untenable or tenuous^{146, 147} should prove most instructive. For in cancer, as in all else, facts do not speak for themselves but must be spoken for.

*In reviewing over 17,000 papers on cancer and related biological subjects the senior author, in the course of the preparation of his text on "The Biological Basis of Cancer," has not found a single valid contribution that fails to find congruence with, and illumination from the trophoblastic or unitarian thesis of cancer.

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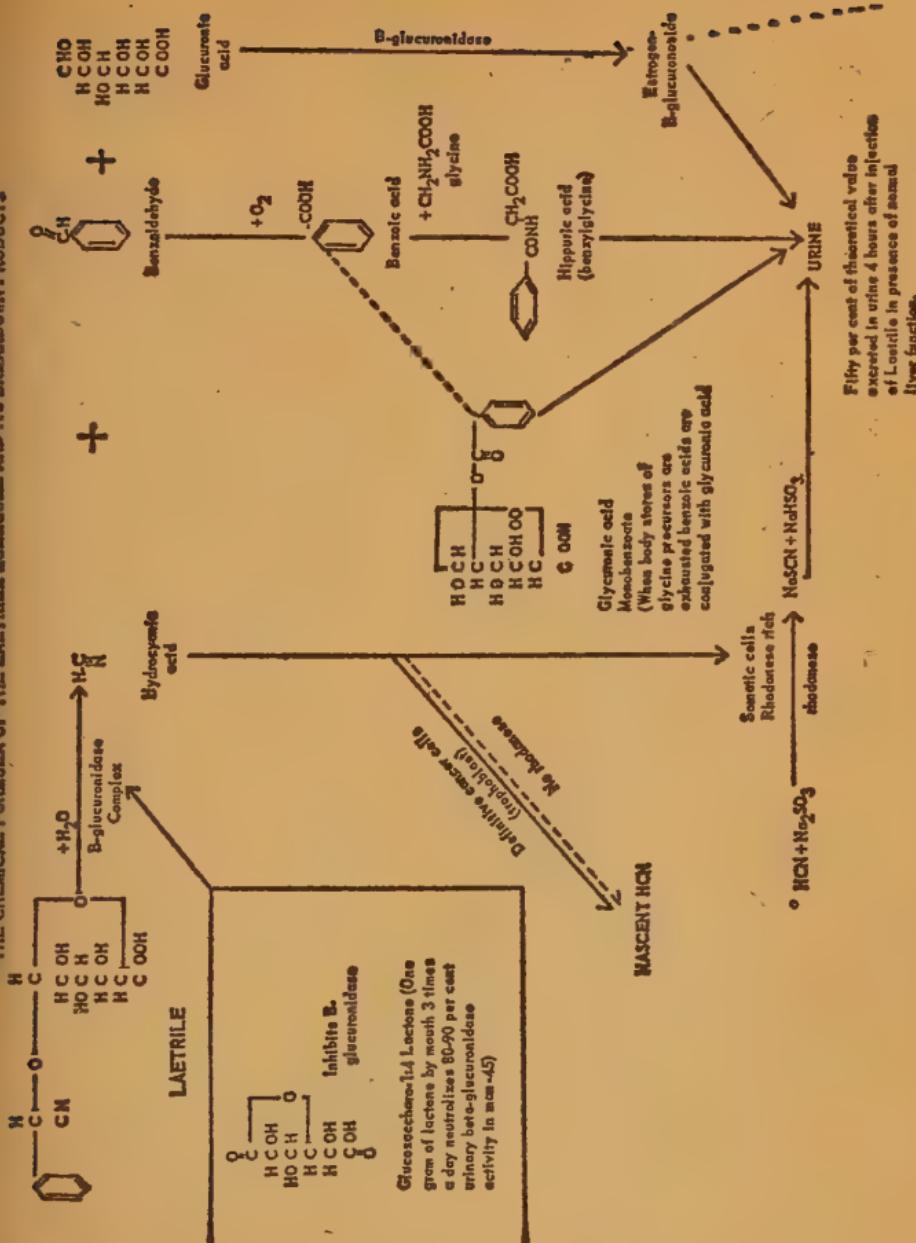
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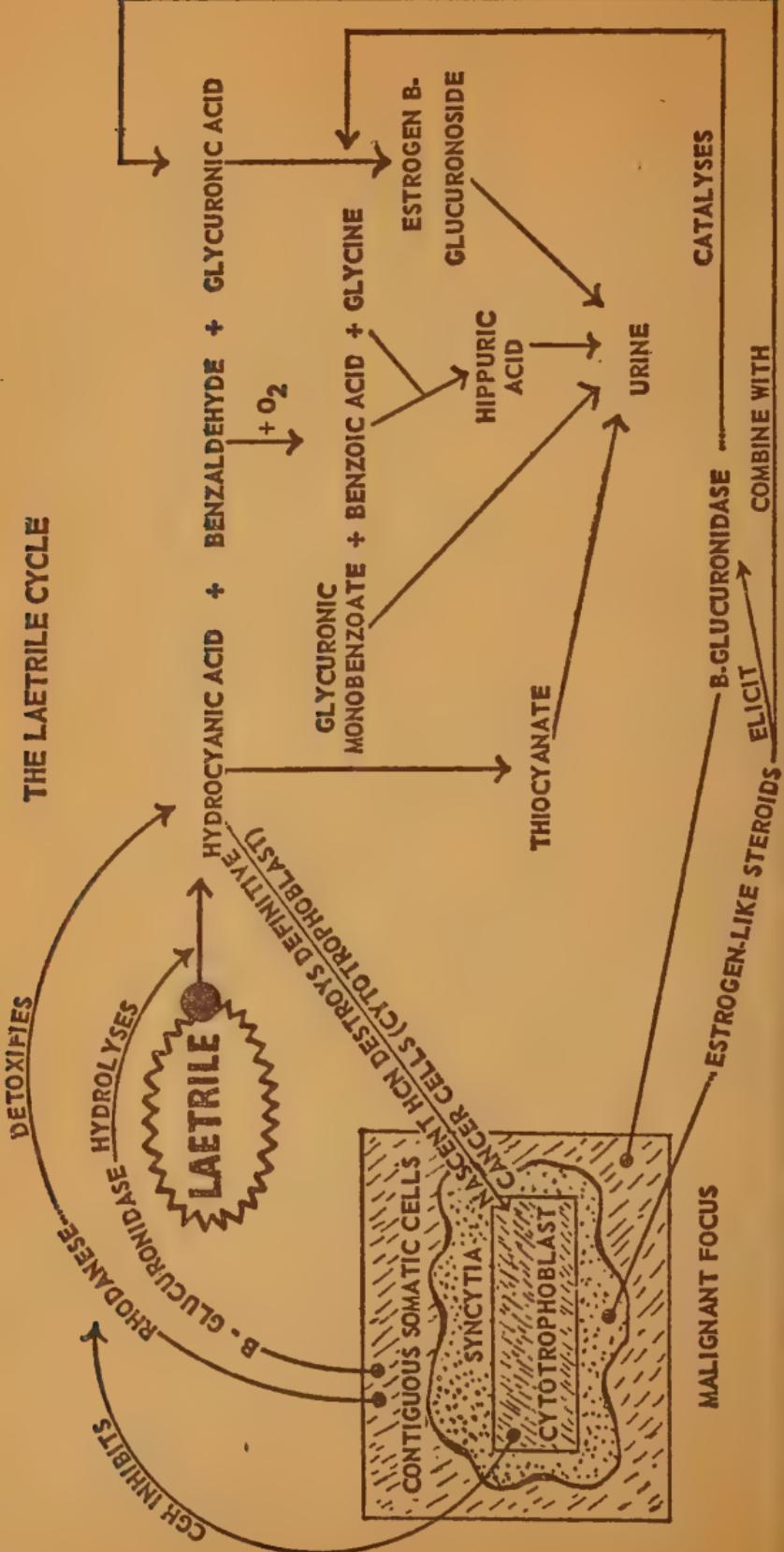
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Note: From 129 to 144 read with an increment of 3.

THE CHEMICAL FORMULA OF THE LAETRILE MOLECULE AND ITS BREAKDOWN PRODUCTS



THE LAETRILE CYCLE



Factors	Origin	Action	End Product
B-glucuronidase(*)	Endogenous in soma Elicited in high concentration at lesion by estrogen- like steroids	Detoxifies estrogen- like steroids Hydrolyzes glucuronides	Estrogen-glucuronoside Aglycon and sugar
Rhodanese(*)	Endogenous in soma Absent in Ca lesion	Detoxifies HCN	Thiocyanate
Chorionic gonado- trophin hormone (CGH)	Produced only by cell- ular trophoblast	Inhibits rhodanese	Unchanged
Estrogen-like steroids	Syncytial trophoblast	Elicit B-glycuronidase	Estrogen-B-glucuronosides from contiguous soma

(*) As enzymes, rhodanese and B-glucuronidase do not terminate in an end product.



CITY OF NEW YORK
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SECRETARY

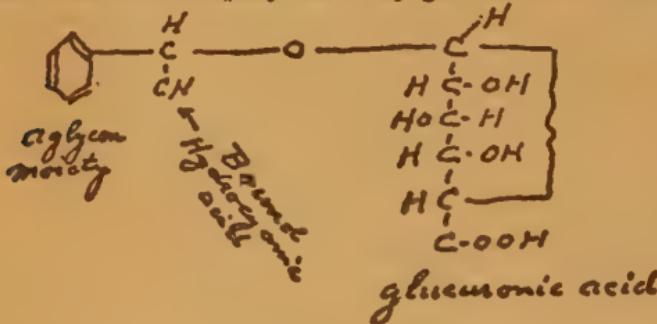
March 10, 1953

Dr. C. R. [redacted]
[redacted]
Newark 2, N. J.

Dear Doctor [redacted]:

Re: The Laetrile Preparation

Before starting the analysis, I thought it would save time to get the structure of the compound. I wrote to the Spicer-Gerhart Company and they gave me the following formulas:



I then proceeded to check up this formula. There is no free Hydrocyanic acid or free cyanide present. It is firmly bound in the molecule.

I then hydrolyzed(broke up) the compound by boiling with HCl under a reflux. On testing for the components produced I found Hydrocyanic acid, glucuronic acid and an aglycon moiety which seemed to be benzaldehyde. My analysis checked the formula given.

The compound can also be hydrolyzed by the enzyme B glucuronidase found in malignant tissue, thus liberating HCN at the site of the tumor.

I hope this will answer your inquiry.

Very sincerely yours,

Alexander A. Gettler
Alexander A. Gettler, Ph.D.

LAETRILE—THE IDEAL ANTI-CANCER DRUG?*

by Manuel D. Navarro, M.D.**

Since Hippocrates described a disease which we now know as cancer, various groups of oncologists have striven to discover a drug for the treatment of this scourge of mankind. The long years have brought to light innumerable drugs claimed to have incredibly dramatic effectiveness against this disease which, however, were proved later by controlled experiments as palliatives only, if not worthless. "Advances in medicine," it is said, "are like salesmen knocking at your door. Hear them before you dismiss them." As a student of bio-chemistry and oncology, I have ventured, therefore, to knock at your portals to bring to your kind attention and tolerance another of these wonder drugs: *Laetrile*, a synthetic drug discovered by Ernst T. Krebs, Jr.¹ which to my mind, training and experience, is the ideal drug for the treatment of cancer!

The term *Laetrile* is used to designate the laevo-rotatory containing glucosides in general and the corresponding glucuronoside in particular. The former are found in plants whereas the latter are synthetic. The glucuronosides differ from the natural glucosides in having for their sugar moiety glucuronic acid rather than an un-oxidized sugar. The purpose behind this difference is to provide a cyanophoric substance during the process of synthesis.

Several papers have reported the presence of impressively high titer of a specific beta glucosidase known as beta glucuronidase in the cancer tissues. This enzyme is normally found in large quantities in the liver; it is also found in the spleen, kidneys and leucocytes; fortunately, none is found in the central nervous system.

The presence of such a high concentration of beta glucuronidase in the liver should mean that it has a function normally in the body. This is precisely the case. This enzyme catalyzes the detoxication of estrogen in the body, causing the conjugation of estrogen with glucuronic acid into estrogen beta glucuronoside which is excreted in the urine.

When the body suffers from cancer the same function is utilized now as a defense mechanism. In fact, the findings of Morrow,

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**Asst. Professor in Bio-Chemistry and Therapeutics, U.S.T.

Greenspan and Carroll² of the low liver and spleen beta glucuronidase concentration in mice with a high cancer susceptibility suggested to them that this factor may be etiologic. For it has been proven that the cancer cell produces large amounts of estrogenic steroids. It was Cori³ who first reported its presence in cancer in 1927. Later, Raudenbusch, Loewe and Voss,⁴ and Geschichter,⁵ and much later, Heiman and Krehbiel confirmed this fact. Finally, in 1944, Roffo⁶ reported the presence of estrogenic steroids in 100% of 1,000 malignant tumors and its absence in 100% of corresponding 1,000 benign tissues.

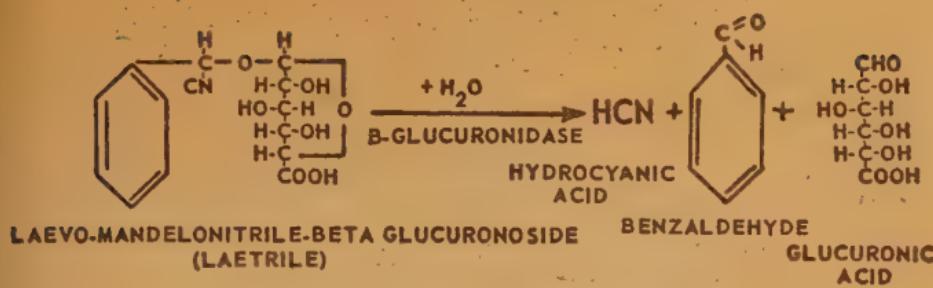
It is well known that, under abnormal conditions, estrogen may be carcinogenic. It is carcinogenic because it is capable of inducing meiosis in a diploid totipotent cell whose unimpeded development results in trophoblast—the ectopic exhibition and persistence of which is expressed as CANCER.

To prevent such a high concentration of estrogen from producing further carcinogenic effects in the body the somatic defenses utilize the beta-glucuronidase as a protective mechanism of detoxication by surrounding the cancer cell with a sea of this enzyme, such that conjugation of estrogen with glucuronic acid into estrogen-beta-glucuronidase takes place right away. This defense mechanism of literally converting the cancer cell into an island encompassed by a sea of beta-glucuronidase may give the impression that it is the cancer cell which possesses a higher titer of the enzyme but such is not the case. The cancer cell being a primitive cell is deficient in most of the complex enzyme systems; in fact, according to Krebs, it does not possess beta-glucuronidase, rhodanese and catalase.

The specificity of beta-glucuronidase for beta cyanophoric glucuronoside has been proved *in vitro* and *in vivo*. In the presence of the enzyme beta glucuronidase, beta cyanophoric glucuronoside is split into one glucuronic acid molecule and an aglycon, the benzaldehyde, and also a molecule of hydrogen cyanide (HCN) which is nascent above 26°C. A 30 mg. dose of *Laetrile* when split by the enzyme is enough to release HCN that would kill a mouse.

The following chemical equation (See Figure 1) shows what happens to the drug after it is acted upon by the enzyme beta glucuronidase:

The cyanide which is liberated around the cancer cell may then enter the malignant cell by diffusion. Destruction of the cancer cell ensues with the combination of the HCN to the iron-containing compounds like the cytochromes of which the cancer cell possesses little, a fact which renders the cancer cell very vulnerable to the poison.



CHEMICAL EQUATION INVOLVED

Figure I

To have an idea of the effectiveness of Laetrile in early cancer let me cite one of the cases reported by Dr. A. T. Harris⁷:

"Miss J. S., a spinster of 36, had '*pre-invasive carcinoma of the cervix*' as shown by two biopsies. Because she was anxious to get married and have children of her own, this patient had refused both surgery—an ideal case for pan-hysterectomy!—and radiation, a good second choice line of conservative therapy. She heard of Laetrile and she asked for that therapy.

"Laetrile was injected directly into the cervix. *In all she received three injections*. Almost immediately she began to improve physically. At the end of the first and second months following Laetrile therapy *biopsies of the cervix were returned negative for cancer*. At the end of the fifth month curettage and a coning of the cervix was done. The pathologist reported:

"Section of the endometrium shows very hyperplastic glands in the proliferative phase. The stroma is quite hemorrhagic. Sections of eight areas, which include the entire 360° cone of the cervix, show numerous cystically dilated endocervical glands together with an infiltration of the stroma by many lymphocytes. There is slight amount of squamous metaplasia near the squamo-columnar junction. There is much squamous epithelium of the vaginal portion present, and there is not the slightest evidence of malignancy present."

One may ask: "Is there no danger of the HCN destroying the contiguous normal cells?" It is true that some of the nearby cells may be affected by the HCN. But should the cancer be found in the liver or other organs rich in *rhodanase or transulfurase*, the normal cells, according to Krebs, escape destruction because this above-mentioned enzyme detoxifies the HCN, forming it into thiocyanates—a mechanism probably provided by nature, one might

say, to take care of possible poisoning from plant foods containing cyanophoric glucosides.

Strangely enough, there are very few systemic reactions from parenteral administration of *Laetrile*. At the present time, these have been observed: mild headache, comfortable drowsiness, mild fever and a slight feeling of weakness which may last from one to three hours. Occasionally, hemorrhage resulting from the destruction of the cancerous growth located in a viscus, like the stomach or urinary bladder may occur.

In 12,000 parenteral doses administered over the past two years no immediate or delayed signs of toxicity have been observed.

Recapitulating, therefore, what are the effects of *Laetrile* observed by those who have used it that makes this drug the ideal anti-cancer drug?

Firstly, the HCN triggered-off from *Laetrile* destroys the cancer cell be it at the primary or metastatic site; slightly affects the contiguous normal cells as explained above. The low cytochrome C concentration in the cancer cell makes it vulnerable to the HCN. Moreover, as Krebs described it, "the destruction produced by *Laetrile* therapy seen at post-mortems is not the massive tissue necrosis sometimes seen in heroic dosages of radiation; rather *Laetrile* leaves us a histological picture showing the necrotic involution of specific cells in a lesion while the functioning or somatic parenchymal elements together with their vascularization and connective tissue investiture remains unimpaired and capable of regenerative proliferation."

Secondly, HCN and benzaldehyde released from *Laetrile* are both powerful analgesic and antiseptic agents, relieving the patient of the excruciating pain and the fetor that is sometimes observed in cancer. Benzaldehyde is oxidized in the body into benzoic acid which in itself is also an antiseptic.

Thirdly, there is observed an increase in appetite of the patient who was formerly anorexic. Also, there is usually a gain in weight.

Fourthly, general increase in a sense of well-being; loss by the patient of those signs and symptoms that readily identify him as a cancer patient.

Lastly, the drug is easily administered by injection either intramuscularly, intravenously or when necessary, directly into the tumor; and there are no severe reactions observed as compared with those seen with the use of other anti-cancer drugs. (Note that *Laetrile* is NEVER given by mouth as the HCL in the stomach is capable of hydrolyzing the drug.)

As a concluding remark, may I say, that if the idea—that in *Laetrile* we truly have an ideal anti-cancer drug—which I have

just brought to your attention comes within your purview of something that is "food for thought", I would consider it sufficient reward for the efforts made in presenting this paper describing for you the action of a drug not yet officially accepted by the medical profession.

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FIVE YEARS' EXPERIENCE WITH LAETRILE THERAPY IN ADVANCED CANCER*

by Manuel D. Navarro, M.D.**

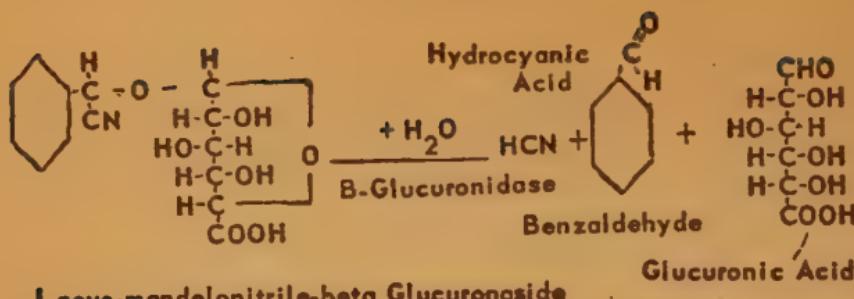
Dr. Charles S. Cameron, medical and scientific director of the American Cancer Society, wrote in his book, "The Truth About Cancer", that the hope for solution of the cure of cancer has to be through drug treatment; while Dr. Isidor S. Ravdin, chairman of the board of regents, American College of Surgeons, believed also that chemistry might provide the cure for cancer because ". . . X-rays and surgery so far have failed." His Holiness, Pope Pius XII, who spoke before a large group of world-known scientists at Castel Gandolfo, in the summer of 1956, expressed the mutual hope that chemotherapy would ultimately provide the cure for cancer.

This hope had its beginning in the works of pioneers among whom are Karczag and Csaba,¹ Crabtree and Cramer,² Maxwell and Bischoff³ and Perry⁴ who all described the regression of experimental cancers of animals following the use of hydrogen cyanide and cyanide salts. Unfortunately the margin of safety between the antiblastic and the lethal dose was so narrow that the use of these cyanide preparations was found impractical.

It was Ernst T. Krebs, Jr. and his co-workers⁵ of the John Beard Memorial Foundation at San Francisco who gave added impetus to the realization of this hope for a cure for cancer with the synthesis of Laetrile. The destructive action of Laetrile on cancer is claimed to be specific: it depends upon the scission of a molecule of hydrocyanic acid, benzaldehyde and glucuronic acid from the Laetrile molecule at the cancer site by the hydrolytic action of Beta-glucuronidase (B.G.) (*See Fig. 1*). The specificity of BG for beta-cyanophoric glucuronoside (or Laetrile) has been proved *in vitro* and *in vivo*. To understand this claim on the specific action of Laetrile on cancer one must recall the physiology of B.G.

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Chemical Equation Involved

Detoxification of HCN:



Fig. 1

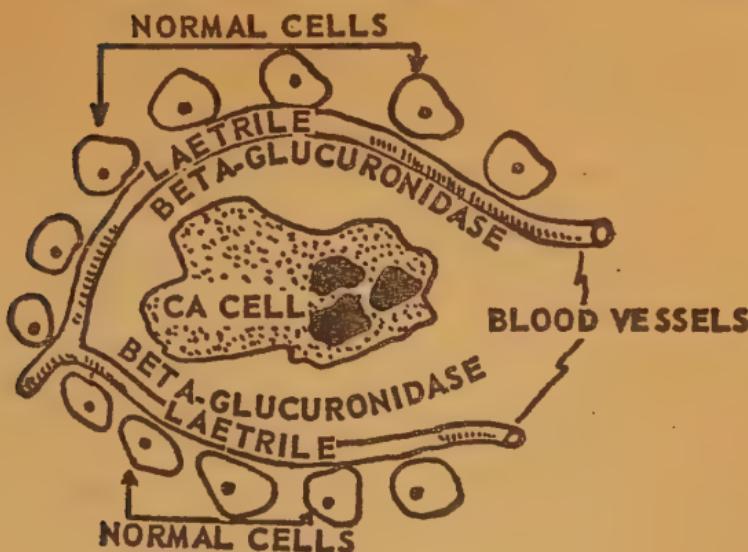
PHYSIOLOGY OF BETA-GLUCURONIDASE

B.G. is found normally in the liver, spleen, kidneys and to a little extent in the leucocytes. B.G. has the function of conjugating estrogen with glucuronic acid to form the estrogen-glucuronoside which is excreted in the urine. In fact, the finding of low liver and spleen B.G. concentration in mice with a high cancer susceptibility suggested to Morrow, Greenspan and Carroll⁶ that this factor may be etiologic. This enzyme, therefore, has the role of performing metabolic detoxication of excessive formation of estrogen or estrogen-like steroids.

DEFENSE MECHANISM IN CANCER

It has been noted as early as 1927 by Cori⁷ that the cancer cell produces large amounts of estrogen-like steroids. This observation was confirmed subsequently by several workers.⁸⁻¹⁰ When the body suffers from cancer this physiological function of B.G. serves as the defense mechanism against excessive estrogen formation by surrounding the cancer cell with a sea of B.G., such that conjugation of the estrogen with glucuronic acid into estrogen-glucuronoside could take place immediately (See Fig. 2). The presence of a high titer of the enzyme B.G. in the cancerous tissues is supported by the observations of several investigators.¹¹⁻¹⁹

Indeed, Sakai,²⁰ Roffo,²¹ and Terrell and Beard²² utilized the presence of chorionic gonadotrophin in the urine as a basis for



DEFENSE MECHANISM

A CANCER CELL IS SURROUNDED
BY A SEA OF B-GLUCURONIDASE

Fig. 2

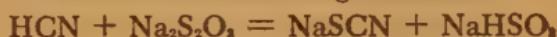
their respective tests for malignancy. The unbelievably very high accuracy of the tests speaks well of this fact—that there really is found estrogen-like steroids in the cancer cells.

This defense mechanism of surrounding the cancer cell with a sea of B.G. would explain why Laetrile is claimed to be specific for cancer—there is a triggering off of a molecule of HCN, benzaldehyde and glucuronic acid from the Laetrile molecule at the cancer site. This mechanism of action brought forward by Krebs has been described in our previous papers.²³⁻²⁴

Hydrocyanic acid is nascent above 26°C, consequently upon the scission of HCN at the cancer site, the toxic gas diffuses into the cancer cell, combining with the iron-containing oxidative enzymes, paralyzing thereby the already defective oxidative process of the cancer cells. The HCN is thus involved in an irreversible chemical reaction with the enzyme of the dead cancer cells.

One may raise the question: "If the HCN diffuses into the cancer cells, can it not affect the surrounding or adjacent normal cells?" The answer is Yes. But the normal cells do not suffer any appreciable injury to their cellular oxidative processes because of the

presence of an enzyme, rhodanase (transulfurase) which converts the HCN, in the presence of thiosulphate or colloidal sulfur into rhodanate or thiocyanate which has hypotensive effect. This enzyme, rhodanase, the cancer cells do not possess. Lang²⁵ gave the detoxication of HCN in the following reaction:



PROOFS OF THE CHEMICAL REACTION

Are there proofs that the reaction as shown by the chemical equation really takes place at the cancer site? The appearance of cyanohemoglobin in the blood several minutes after Laetrile injection is proof of the scission of HCN from the Laetrile molecule. But the therapeutic effects themselves as observed would be the other proofs of such scission of HCN in the cancer site, viz:

1. *Destruction of the tumor:* The anti-blastic effect of Laetrile mirrored by the diminution in the size of the tumor or its complete regression was noted in 20%. The effect could be dramatic if the tumor were small in size and recent. But in far advanced cases or large tumors, there may be slight diminution in size after one or two months of Laetrile therapy. However, metastatic glands disappear completely or become very small. In those cases which have reached the "point of no return," no such diminution was noted.

Hemorrhage occurring some hours after the injection of the drug was seen rarely. Such cases were those cancers involving the G-I tract, urinary bladder and the lungs. Of course, bleeding occurs in tumors of these organs even without treatment, so that Laetrile therapy, if one fears the bleeding as an effect, should not be a contra-indication in these cases. Krebs suggested that smaller doses of Laetrile be used to produce more connective tissues around the cancer site which would minimize subsequent hemorrhages at that area.

Pyrexia was noted after Laetrile injection in a few patients. This may be attributable to subsequent rapid absorption of the proteins from the necrotic cancer tissues..

2. *Analgesia.* HCN and benzaldehyde are potent analgesics. Pain in cancer may be relieved for as long as four days by a single injection of 250 mg Laetrile. This effect was consistently observed in most of the patients except in a few who had undergone previous deep X-ray therapy. The pain produced in these irradiated patients would seem to be due to the resulting fibrosis so that the release of HCN at the site of pain could not take place because there would be no sea of BG to hydrolyze the Laetrile. Quite often

the patients who had reached the point of no return were made more comfortable during their last days. Often times the patients preferred the analgesic effect of Laetrile to that produced by the opiates because with Laetrile they did not go to sleep when it was administered during the daytime.

3. *Fetor* resulting from the secondary infection in ulcerated carcinomas was relieved. In the few cases with fetor, this symptom was relieved by topical application of Laetrile solution, confirming therefore the observations of Guidetti;²⁶ while those with internal cancers, parenteral administration of Laetrile took care of the associated fetor. This therapeutic effect is again explained by the release of HCN and benzaldehyde at the cancer site, the latter being readily oxidized into benzoic acid. Both compounds are excellent antiseptics.

4. *Appetite* improved where anorexia was observed with subsequent gain in weight. It would seem that before the CN- radical could combine with an H⁺ to form HCN, cobalt and a protein molecule unite with it to form a molecule of cyanocobalamin (vitamin B₁₂). Wooley²⁷ gave evidence that vitamin B₁₂ can be synthesized by cancer cells. It would appear that this synthesis of cyanocobalamin is a defense mechanism of the cancer cells against destructive agents. This synthesis of cyanocobalamin would be significant because this vitamin is presumed to stimulate mitosis. Consequently, folic acid and vitamin B₁₂ should never be administered to cancer patients.

Incidentally, Kleiner, Black and Bolker²⁸ demonstrated that cancer cells could adapt themselves to compounds destructive to them; these investigators showed clinically that sodium fluoride, iodoacetic acid, malonic acid and sodium azide could reverse this adaptability of the cancer cells by giving these compounds at intervals. Our limited observations and those of Dr. Shigeaki Sakai²⁹ of Matsuyama City, Japan, would seem to show that Laetrile combined with other anti-cancer drugs (Thio-tepa or Azan) produced synergistic and more dramatic therapeutic effects.

5. *Hypotensive* effect was noted in hypertensive patients suffering at the same time from cancer. Cases I and V had systolic blood pressures of 200 mm and diastolic readings of 100 mm. With Laetrile therapy the blood pressure was maintained at 140 or 150/80 which effect was never satisfactorily produced by any of the hypotensive drugs given them.

DOSAGE

One hundred mg Laetrile is dissolved in 5 cc normal salt solu-

tion (the 250 mg dose is dissolved in 8 cc and the 500 mg in 10 cc). Administration may be hypodermically, intramuscularly, intravenously, intraperitoneally or intrapleurally. In ulcerating carcinomas the powdered Laetrile may be incorporated in an ointment for local application, or the Laetrile solution may be used to saturate the gauze applied over the ulcerated growth.

To enhance the hydrolysis of Laetrile, 100 mg or 200 mg of BG is dissolved in 3 or 5 cc N.S.S. and injected intramuscularly, thirty minutes after the Laetrile injection. Occasionally the BG may be infiltrated around the tumor and 30 minutes later the Laetrile injection is administered intramuscularly. A separate syringe should be used always for the BG to avoid the possible reaction taking place in the syringe itself when only the needle is changed. Both the Laetrile and the BG injections are given every 72 hours. There are times when the case is so far advanced that this interval may be made every 48 hours.

An adjuvant to Laetrile therapy is the administration of 5% Dextrose in Lactated-Ringer solution³⁰ on the day of the Laetrile injection. The aim behind this is the lowering of the pH of the tumor to about pH 6 at which concentration of the hydrogen ion scission of HCN from Laetrile is at optimum.

Occasionally Laetrile may be administered also by iontophoresis. Krebs and Harris³¹ have noted very good results with this form of therapy especially in breast cancers. Our experience on this method of administering Laetrile is limited.

Laetrile therapy may be discontinued after the Beard Anthrone test has become negative. However, a concluding series of injections of chymotrypsin be given with the end in view of digesting whatever malignant cells remain. This was advocated as a form of treatment by John Beard³² as early as 1911. The number of cases the author has treated by this enzyme treatment is very limited. But it would seem to show that the digestive effect of chymotrypsin is synergistic with the destructive effect of Laetrile. Eighteen mg of crystalline chymotrypsin is dissolved in a suitable solution for venoclysis like Dextrose 5% and is given daily for ten days.

TOXICITY AND SENSITIVITY

Though prolonged Laetrile therapy did not produce any sign of toxicity, sensitivity to the enzyme was noted in four cases. The few cases that were sensitive to the enzyme were all obese. The symptoms noted immediately or after a few hours following BG administration were: coughing, a sense of suffocation, pain at the lumbar region, collapse which necessitated the use of analeptics and lastly,

the production of urticaria that progressed to bleb formation.

There is no toxicity when Laetrile is given parenterally. This is a great advantage over all other known anti-cancer drugs. It should never be given by mouth because the HCl is capable of hydrolyzing the Laetrile. In two patients on whom we have administered Laetrile for over a year no immediate or delayed signs of toxicity have been observed. That Laetrile is non-toxic when given parenterally may be observed in cancer bearing patients (*Case IV*).

Summing up the author had treated a total of 83 patients with Laetrile and chymotrypsin. Laetrile and B.G. or Laetrile with B.G. and chymotrypsin. *Table I* shows the break-down of these Laetrile

TABLE I
BREAK-DOWN OF CASES TREATED

Ca, Breast	17	Ca, Max. Antrum	3
Ca, Stomach	11	Ca, Liver	3
Ca, Lungs	11	Ca, Thyroid	2
Sarcoma	10	Lymphoepithelioma	2
Lympho	7	Ca, Cerv. Gland	1
Fibro	2	Ca, Esophagus	1
Spindle cell	1	Ca, Pancreas	1
Ca, Cheek, Tongue	8	Epi.-Ca, Uterus	1
Ca, Larynx, Nasopharynx	5	Hemangioma, neck	1
Ca, Rectum, Colon	4	Hodgkin's Disease	1
		Hypernephroma	1

Total: 83

treated cases. One third of them received 2,000 mg or more of Laetrile. The length of time of survival ranges from 7 to 24 months.

REPRESENTATIVE CASES

Case I: Diagnosis: Adenocarcinoma, left breast.

F.S., 53, single, noted a mass in the left breast in 1951. In three years her ailment became worse. She had dizzy spells and fits of coughing; her weakness became more marked and she continued to lose weight. "Rheumatic" pains bothered her continuously for which reason she was bed-ridden for the entire duration of 1956. In November 1956 she was brought to the hospital in a comatose state, presenting uremic-like symptoms. Blood pressure was 200/100. There was a right sided spastic hemiplegia, a low grade

fever of 37.3°C that lasted five days. Urine analysis showed one plus albuminuria. The mass in the left breast measured 3 inches in diameter, hard in consistency and occupied the outer left upper quadrant, encroaching upon the rest of the mammary tissue. The nipple was retracted upward, laterally; the skin showed the characteristic "orange-peel" appearance. Glandular enlargements were seen in the left supra-clavicular fossa and along the left axillary fold.

She had hemoptysis on the 4th hospital day. The sputum was negative for acid fast bacilli. X-ray examination of the chest showed: "Malignant, neoplastic process, metastatic, advanced, both lungs." The pelvis revealed "advanced bony destructive changes, around both hip joints, involving proximal end of right femur, and probably also left proximal femur, metastatic, malignant."

Treatment:

Laetrile, 100 mg was administered intramuscularly. Thirty minutes later B.G. 100 mg was injected intramuscularly. Also given daily for 13 days was 5% Dextrose in Lactated-Ringer solution. A total of 975 mg of testosterone was also given aside from two ampules of iodoseptine and Serpasil tablets, 25% Dextrose and Super-bee.

Effect:

After the first injection, the patient was able to sleep better. On the third injection, the spastic fingers and toes of the right limbs could move or wiggle. An "orange-peel" erythematous area of about 4 inches in diameter on the right iliac crest subsided and soon became normal in texture and appearance. The patient left the hospital on the 13th hospital day much improved. After the fifth injection she could make the Sign of the Cross. The appetite which was formerly poor was very good by this time. Her memory and mental alertness returned to normal. Coughing which was formerly very frequent became much less in number. The pain at the right hip joint subsided. By the time the eighth injection of Laetrile was given she could eat alone, unaided. After the tenth injection, she could turn in bed by herself and sit up alone unsupported. Her tonsils which were enlarged before the start of Laetrile therapy were now back to normal size. Her troublesome external hemorrhoids became very small and ceased to bleed; the pain had also subsided completely.

By the fifteenth injection, she was learning to stand up with somebody's help. The metastatic glands over the left axillary area

and the left supra-clavicular fossa had both disappeared completely. After the 18th injection she was walking a few steps.

Radiography of the *chest* taken two months later showed the "numerous rounded densities seen diffusely scattered in both pulmonary fields in previous examinations of Nov. 11, 1955, have apparently undergone almost complete reabsorption. Only a few small residual patches were seen at both bases, slightly larger in the left, and in the right upper lung field. *Pelvis:* The advanced bony erosive changes in both iliac bones and in the right ischial bone around the hip-joint show evidence of definite bone regeneration and repair."

By the middle of February, 1956, she was already walking longer distances. Her cough had ceased altogether. She had gained twenty pounds. In March, 1956 she was already pottering in her garden and occasionally did her own cooking. The blood pressure had gone down to 150/80. Serpasil had not lowered her blood pressure consistently until Laetrile was also administered. The tumor in the left breast had become fibrotic and the "orange-peel" appearance of the breast was barely noticeable, but the nipple still remained retracted upward probably as a result of the fibrosis.

After receiving a total of 40 injections of 100 mg of Laetrile or an equivalent of 4,000 mg, a radiological check-up revealed the following findings:

Chest—"There appears to have been a slight further reabsorption and further definite fibrotic reaction since last examination (Jan. 12, 1956). The numerous rounded densities seen throughout both pulmonary fields in the first examination (Nov. 12, 1955) are now almost completely gone.

"A few tiny rounded residual shadows are still discernible, but with difficulty. The preponderant picture is that of pulmonary fibrosis."

Pelvis: "The extensive bony destructive changes in both iliac and in both ischial bones and at the proximal end of the right femur have apparently undergone almost complete repair.

"The previously badly eroded outlines of the pelvic bones now appears repaired, with intense osteosclerotic reactions in the iliac bones and around the hip-joints, more in the right side, and at the superior edge of the great trochanter of the right femur. There seems to be still some residual rarefied areas.

"A slight residual deformation of the symmetry of the pelvic brim is seen around the right hip-joint."

Latest radiological check-up showed no apparent change. The patient after 20 months was still living. On the 24th month she died of acute intestinal obstruction.

Case II: Diagnosis: Hodgkin's Disease.

J. de G., 50, female, had undergone irradiation of the cervical, sub-maxillary, axillary and inguinal lymph glands. These glands responded well to the deep X-ray therapy. When she was seen after the irradiation, she had a remaining unirradiated lymph gland, 1½ inches in diameter, found at the popliteal fossa of the right lower extremity. This was the target for the Laetrile therapy. A temperature of 39° C was observed nine hours after the first injection. Following the second injection of 100 mg Laetrile, she had again fever of 39° C which lasted for a week. Subsequent examination of the popliteal fossa revealed total disappearance of the malignant gland. The hyperpyrexia would seem to be due to the effect of the absorption of proteins from the destroyed malignant lymph gland located at the popliteal fossa of the right lower extremity where drainage to the outside was not possible. With the high fever, the patient had also generalized pruritus. After seven months the patient was still living. It was at this time that she developed jaundice from which she recovered subsequently.

Case III: Diagnosis: Epidermoid Carcinoma, Grade IV, nasopharynx.

B.C., 66, male, had a large nasopharyngeal tumor which had metastasized to the left cervical lymph glands and to the brain. His chief complaint was severe left sided headache of 16 months duration. He had blurring of vision, dysphagia and epistaxis four months before admission. Three weeks before entry into the hospital he had four bouts of projectile vomiting.

There was V, VI, IX and X cranial nerve involvement as shown by the hyperalgesia of the first division of the V, left abducens paralysis, deviation of the uvula to the right and protrusion of the soft palate downward on the left side. The left eye was closed and the left pupil was eccentric and immobile. The patient stayed in bed most of the time with an ice-cap on the left side of the head. Radiography showed the following findings: ". . . in the submento-occipital or basal position there is a soft tissue mass obscuring the left side of the sphenoid and obliterating the same region. There is evidence also of bone destructive changes."

The first injection of Laetrile relieved him of the headache immediately for a few hours. The second produced a more marked diminution of the intensity of the pain which had now localized at the parieto-temporal region of the left side of about 5 cm in diameter. After the third injection the left eye could be opened for a much longer time unlike before when it was always closed.

He had also dispensed with the icecap. Infiltration of the cervical gland with B.G. four times at four days interval, followed with intramuscular injection of Laetrile thirty minutes later had caused the gland to become small and fibrotic. Subsequent injections of Laetrile relieved him of the pain to a considerable degree so that he could walk around in the ward chatting with his ward-mates. An evaluation of the nasopharyngeal growth after two months of Laetrile therapy showed that the mass has decreased in size by one-third; there was less tendency to bleed when touched. Laetrile therapy had apparently no depressant effect on hematopoiesis as shown by two blood examinations. *July 25, 1956:* Hb: 9 Gm%; RBC: 3,760,000; WBC: 5,900. Differential count: Plynuclears, 66% (stabs 4% and seg. 62%); Lymphocytes, 29%; Eosinophils, 4% and Mononuclears, 1%. *August 22, 1956:* Hb: 9 Gm%; RBC: 3,350,000; WBC: 8,650 Differential count: Polynuclears, 38% (stabs 7% and seg. 31%); Lymphocytes, 53% and Eosinophils, 9%. The patient left the hospital considerably and remarkably improved. A total of 2,100 mg of Laetrile and B.G. were given him. On the day of Laetrile injections he received also 500 cc of 5% Dextrose in Lactated-Ringer solution.

Case IV: Diagnosis: Ductal cell carcinoma, left breast. Pregnancy.

C.D., 39, female, underwent a radical mastectomy two years before and the cancer had now recurred. She was three months pregnant. She suffered pains in the right hip and leg. She was placed under testosterone therapy for 1 month but it was ineffective: the cancerous process continued to spread—to the right breast, axillary lymphatic glands, and the brain. Radiography showed erosions of the 2nd and 3rd ribs of the right side, osteoporetic changes were noted in the pelvic and femoral bones. She was therefore placed under Laetrile therapy. The relief from pain was immediate. The dose given at first was 100 mg and it was increased later to 250 mg because the cancerous process was found to be widespread. Injection was at first intramuscular but later it was given intravenously; treatment lasted four months. Treatment of the right breast with Laetrile by iontophoresis was attempted but the result obtained was not so good as the amount of Laetrile applied was 125 mg only. On the 8th month of the pregnancy the patient was induced into labor and a live baby girl was delivered. Because the mother was markedly anemic and much weakened by the malignant disease and the super-human efforts of delivering her baby, she finally died 16 hours after. This case is presented to show the

non-toxic action of Laetrile even when administered intravenously in pregnant patients.

Case V: Diagnosis: Hypernephroma, left kidney.

D.M., 49, female, was admitted to the hospital with symptoms of bronchiectasis for which she was being treated. She had a large mass in the left hypochondriac and lumbar region which was thought might be the spleen because she had a history of having had malaria. A blood examination done following an attack of chills was negative for malarial parasites.

Her blood pressure was 200/100. Despite the anti-biotic therapy, the densities of the lung fields continued to increase so that the possibility of cancer was entertained now. On July 9, 1956 examination of the urine with the Beard Anthrone test was positive for malignancy. Laetrile therapy was started at a dose of 100 mg every 72 hours. The chest pain was relieved somewhat by the first injection. The blood pressure readings were observed to lower from day to day with subsequent injections of Laetrile until the systolic and diastolic reading stayed around 140/80; the associated headache was also relieved.

Her coughing was relieved slightly. At this time she had hemoptysis. The bleeding was controlled with pituitary extract diluted in 10 cc NSS given intravenously very slowly so that the whole injection took 15 minutes to administer. The patient improved considerably so that she was able to go home for a vacation. After two months she had hematuria. This gave the first suspicion that the kidneys might be involved. On her return to the hospital a pea-sized lymph node on the left third interspace close to the sternum was excised and the biopsy revealed hypernephroma, metastatic. This verified the Beard Anthrone test which was positive five months earlier. Retrograde pyelography revealed a large left kidney that was poorly functioning. The radiologists were afraid to combine Laetrile therapy with deep X-ray therapy so the latter alone was the treatment decided upon for her. But unfortunately she did not respond very well to the irradiation as was expected and she died some two weeks later. A total of 6,000 mg of Laetrile and B.G. were given to her.

Case VI: Diagnosis: Lymphocytic lymphosarcoma, cervical glands and scalp.

M.O., 9 years old, female, had cervical lymph gland enlargement and thickening of the scalp. The suspicion of tubercular infection was disproved by the biopsy. She was started on Laetrile therapy

by having the middle gland composing a group of three big glands infiltrated with B.G. 100 mg. One hundred mg Laetrile was injected in the buttock thirty minutes later. After four such infiltrations with B.G. the middle gland disappeared and only the two untreated glands remained. Because of the difficulty of injecting B.G. into the scalp, X-ray therapy was decided for that area. The scalp responded very well to the tangential irradiation. A total of 900 r for the left side and 1,050 r for the right were administered. After the series of irradiations, the blood picture changed "overnight" into a leukemic blood picture. This case is presented to show the effect of infiltrating the lymph gland with B.G. and the implication of the effect of deep X-ray therapy on lymphosarcoma. Other patients on whom we have done this technique of infiltrating the lymph gland with B.G. did not turn leukemic. The administration of vitamin B₁₂ might be implicated in this case. Pathologists believe that the patient had always been leukemic but did not have any blast cells in the peripheral blood. Unfortunately no bone marrow examination was done on this case before the start of treatment which could have clarified the diagnosis. A hematologist took over the case to try an antileukemic drug but the patient left the hospital before she could start the treatment.

Case VII: Diagnosis: Epidermoid carcinoma, forehead.

G.M., 50, male, had in 1942 a tiny eruption on the forehead that did not heal. Subsequently, a biopsy of the lesion revealed the malignant process that it was. Soon this growth grew bigger and metastasized to the frontal bone. Excision of the affected portion of the skull was done and with plastic surgery the exposed meninges were covered up. After three months the malignant process had also spread to the surrounding areas. By 1956 when the author saw this patient the carcinoma had eroded part of the left supra-orbital bone, invaded the brain, eaten up most of the right mandible and burst open out of the right cheek and then spread to the right chain of cervical glands. He had a concomitant pulmonary tubercular infection as proven by a positive sputum examination. The ulcerating areas were emitting a very foul odor. The areas away from the buccal cavity were covered with gauze saturated with Laetrile solution and in twenty-four hours the odor had disappeared; while those untreated portions were still emitting very foul odor. He was suffering from severe headache which could hardly be relieved by analgesics. But with the administration of 100 mg Laetrile, the headache was relieved and the patient

could spend the day comfortably, reading newspapers or listening to the radio. But this patient's condition had reached the "point of no return". Ultimately, the malignant process of the brain soon became manifest; hemi-plegia set in and he died not long after.

Case VIII: Diagnosis: Carcinoma, stomach.

P.D., 50, male, showed a filling defect on the lesser curvature. A mass could be palpated at the left hypochondrium and a solitary lymph node was present at the left supraclavicular fossa. Appetite was very poor. Laetrile therapy was instituted combined with 18 mg Chymotrypsin dissolved in 5% Dextrose in lactated-Ringer solution 500 cc. After three such injections the mass at the left hypochondrium could hardly be palpated. Two physicians and a surgeon who had examined him previously attested to this fact because a second surgeon could hardly appreciate the enlargement mentioned in the clinical history. Also the size of the lymph gland on the left supraclavicular fossa had regressed from a size measuring 1 inch in diameter to less than $\frac{1}{4}$ inch. Unfortunately the treatment of this patient was cut short by a fatal coronary attack, probably brought on by a metastatic embolus. The combined therapy of Laetrile and Chymotrypsin seemed to exert synergistic effect. The size of the tumor had regressed dramatically after three injections of both drugs.

Case IX: Diagnosis: Papillary adenocarcinoma, thyroid.

J.A., 79, female, noticed after 39 years that her goiter had grown and become three, as if there were two daughter goiters, one on each side of the big thyroid gland. In 1954 there was pain in the left side of the occiput and a bulging soon appeared at that area. Every time she moved her head there was a splashing sensation and pain was also felt. Because of her advanced age and the extent of the metastatic process, surgical intervention was deemed unwise. Laetrile therapy was therefore instituted. The first injection given her relieved the pain in the left side of the head. Soon the splashing sensation was also much less. Measurements of the thyroid glands and the cranial metastasis showed slight diminution after two months of treatment. Pain in the head, however, had practically disappeared. At one time the beta-glucosidase was injected into the right "daughter" gland of the thyroid and she suffered a severe reaction, characterized by pain in the lumbar region and difficulty of respiration. After two or three minutes she felt better. No treatment was needed for her reaction. Subsequently B.G. injections were made intra-

muscularly and she has had no further reactions. Diminution in size of the tumors was rather slow. This case is presented because Laetrile treatment was given for eleven months without any untoward effect except when B.G. was injected directly into the thyroid gland. The patient is still living after three years.

SUMMARY AND CONCLUSIONS

In 1952 Ernst T. Krebs, Jr. and co-workers described the synthesis of a cyanophoretic compound called Laevo-mandelonitrile glucuronoside, or Laetrile for short. Laetrile is claimed to be specific for cancer. This claim may be better understood by recalling the physiology of the enzyme Beta-glucuronidase. This enzyme hydrolyzes Laetrile into HCN, benzaldehyde and glucuronic acid at the cancer site. The HCN triggered-off diffuses into the cancer cells, combining with the oxidative enzymes, paralyzing thereby the already defective oxidative processes of the cancer cells. The mechanism of action of Laetrile and the chemical equation involved are presented.

The therapeutic effects observed by the author in the advanced cases of cancer under Laetrile therapy which may be taken as proofs of the chemical reaction produced at the cancer site are as follows:

1. The anti-blastic effect mirrored by the diminution in the size of the tumor or its complete regression was noted in 20%. Hemorrhage occurring some hours after the injection of the drug was observed rarely.
2. Analgesia was consistently noted in most of the patients except in a few who had undergone previous deep X-ray therapy.
3. In the few cases wherein fetor was observed, this symptom was relieved by topical application of Laetrile solution in ulcerating carcinomas, while parenteral administrations took care of the fetor associated with internal cancers.
4. Appetite improved where anoxeria had been observed with subsequent gain in weight.
5. Hypotensive effect was noted in hypertensive patients suffering at the same time from cancer.
6. Pyrexia was seen after Laetrile injection in a few patients.

Though prolonged Laetrile therapy did not produce any sign of toxicity, sensitivity to the enzyme was noted in a few cases.

Based on our unpublished observations it is very likely that in early cases of cancer Laetrile may truly be *curative* but certainly *palliative* in far advanced cases.

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LAETRILE THERAPY IN CANCER*

by Manuel D. Navarro, M.D.**

Since the last report on Laetrile (nitriloside) therapy for advanced cancer at the International Union Against Cancer Symposium on Cancer Chemotherapy for the Pacific-Asian Area in Tokyo in 1957¹—the dosage of Laetrile (nitriloside) has considerably been increased. In 1953 it ranged from 50-100 mg; in 1957, 250-500 mg and the most the writer gave to patients who have benefited from the drug was a little over 2 grams. Now, the dose ranges from 1,000 to 2,000 mg intravenously daily and as much as 3,000 mg for a minimum total of 30 grams—a dose considerably greater than what the writer or the others have used in 1952.

It would seem that there is some degree of parallelism between penicillin and Laetrile (nitriloside) as regards dosage. When the former was found excellent for several infections caused by Gram-positive or Gram-negative microorganisms, it was reportedly a *failure* in sub-acute bacterial endocarditis at the routine dose of 100,000 Units, until a Brooklyn physician thought of administering ten times this amount.² True enough, the 1,000,000 Units of penicillin proved effective in sub-acute bacterial endocarditis with the subsequent saving of thousands of patients destined to die from this disease. That the same experience on an increase of the dose for the maligned Laetrile (nitriloside) for cancer therapy holds true is borne out by the work of the Canadian investigators, pioneers in the use of the massive dosages of this drug.³ It is very fortunate that the Beardian scientists can exchange data for each benefits from the findings of the others.

Since the mechanism of the action of Laetrile (nitriloside) is one of the ways of understanding the claims for the effectiveness of this drug in cancer, a cure for which is so desperately needed and for which the world is spending hundreds of millions of dollars, let us discuss this mechanism briefly.

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The antiblastic action of Laetile (nitriloside)* depends upon the scission of the molecule to a molecule of hydrocyanic acid, benzaldehyde and a sugar or its acid through the hydrolytic action of beta-glucosidase and/or beta-glucuronidase (BG)**. The specificity of BG for the natural nitrilosides (Laetiles) or beta cyanophoric glucosides and glucuronosides or the synthetic Laetiles [nitrilosides] has been proved *in vitro* and *in vivo*. To understand the hydrolytic action produced one must recall the physiology of BG which is tied to the Beardian thesis of cancer.

BG is found normally in the liver, spleen, kidneys, and to a certain extent in the leucocytes. It has the function of conjugating the estrogen with glucuronic acid to form estrogen-glucuronoside which compound is excreted in the urine. BG is therefore responsible for the metabolic conjugation of any excess of estrogen-like steroids present in the body.

Since Cori⁴ reported in 1927 on the presence of large amounts of estrogen-like steroids in cancer, other investigators have confirmed his findings.⁵⁻⁷ Such excess formation of estrogen-like steroids in cancer therefore brings into play the physiologic role of BG to serve as the catalyst for this defense mechanism. Consequently, the body causes the area where the excessive steroid formation occurs to be surrounded by a sea of BG. Such presence of a high titer of BG in cancer tissues is supported by the observations of several investigators foremost of whom are Fishman and Anlyan.⁸⁻¹¹

Such defense action of surrounding the cancer cell with a sea of BG is responsible for the specific action of Laetile (nitriloside). Parenteral administration of the drug results in the hydrolysis of the Laetile (nitriloside) molecule (Laevo-mandelonitrile glucuronoside) at the cancer site by BG into HCN, benzaldehyde, glucose and/or glucuronic acid.

HCN being nascent above 26°C. will, upon its release from the Laetile (nitriloside) molecule, diffuse into the cancer cells causing their death; while the normal body cells adjacent to the cancer cells would not succumb to the lethal effect of the hydrocyanic acid because of the presence of rhodanese—absent or deficient in the cancer cells—which converts the poison into thiocyanate, a compound with hypotensive action. The writer has

*Anitriloside or Laetile is any cyanophoric glucoside and/or glucuronoside that when exposed to beta-glucosidase and/or beta-glucuronidase (BG) is hydrolysed to an aglycon, nascent hydrogen cyanide, and a sugar or its acid.

**BG refers to the complex of beta-glucosidases, beta-glucuronidases and other enzymes generically comprising the beta-glucuronidase focally characterizing a malignant lesion.

noted this hypotensive action following Laetrile (nitriloside) injections in several cancer patients suffering at the same time from hypertension.

One distinct advantage of this drug over all other anti-cancer drugs currently under investigation is that it does not depress the bone marrow and can therefore be administered for quite a long period of time.

Several cases of early cancer given this form of therapy are still alive for as long as 74 months, while the survival of the far advanced cases has been increased significantly as compared with the controls which did not receive Laetrile (nitriloside). One of the means of knowing when to stop or resume this form of therapy used by all Beardian scientists is the Beard Anthrone test (BAT), a modification of which was presented at the last cancer congress held in London in 1958. Several of the illustrative cases using the different doses that went hand in hand with the development of Laetrile (nitriloside) therapy are described below:

ILLUSTRATIVE CASES

A. 100 mg dose:

Case 9: A.G., 78, widow, underwent a simple mastectomy for a mass in the left breast that was benign to needle biopsy. The histological section, however, revealed adenocarcinoma. The BAT was ++. Two months after the operation the patient noted lymphadenopathy in the axilla with concomitant pain, itchiness and redness over the mastectomy scar. The BAT was still positive. On March 14, 1956 she was injected Laetrile (nitriloside) (100 mg) every four days for eighteen doses. Beta-glucosidase was an adjuvant then. With the injections, the patient was relieved of the pain, the itchiness and redness along the scar disappeared also. After the 12th injection, Laetrile (nitriloside) was also administered by *iontophoresis* for a total of six applications over the axillary lymphadenopathy resulting in the disappearance of the mass, leaving only a small fibrotic nodule. Up to the present -74 months after Laetrile (nitriloside) therapy was instituted—the patient is feeling well with no recurrence of her malignant condition. The BAT is negative.

B. 250 mg dose:

Case 19: R.P., 27, single, had a +++ BAT after undergoing pan-hysterectomy. After her operation she still had hypogastric and sacro-lumbar pains and melena. Because of the positive BAT, she received post-operative irradiation and later when the urine

persistently showed positive results with the BAT, Laetrile (nitriloside) (250 mg) injections every four days for three months were given. The injections relieved her of the hypogastric and sacro-lumbar pains. The BAT became less positive as the treatment progressed. Because she felt so well she stopped all therapy for two months but resumed her injections when the BAT was shown to be still positive. Finally, in February 1959, exactly a year after her operation, the BAT became negative. She is healthy and strong and presently works as secretary for a commercial firm 29 months after Laetrile (nitriloside) therapy.

C. 250-500 mg dose:

Case 68: C.B., 30, female, underwent a series of nasal operations since 1955 for the chief complaint of nasal obstruction. The first four operations were found benign in character, or at least the characteristic histological picture of malignancy were not yet evident. In all she had five operations, the last one was done in December 1958 when the excised specimen was finally reported as malignant: "Transitional cell" carcinoma. The BAT was positive at this time. She underwent radiation therapy. In June 1959 she had a recurrence of the nasal obstruction and accompanied now by bulging over the right maxillary antrum. The BAT was still positive. Biopsy was done again and the report was still the same: "transitional cell" carcinoma. The patient has refused further surgical treatment but agreed to try deep X-ray therapy and Laetrile (nitriloside) injections (she started with 250 mg and then received a few 500 mg doses). The bulging on the right antral region disappeared during the course of treatment while the pain and the nasal obstruction were relieved. The six months of relief previously obtained with surgery and radiation therapy was now stretched to 1½ years by radiation and Laetrile (nitriloside) therapy. Although she was symptom-free, the BAT was still positive. In January 1961 she became aware of the presence of pea-sized nodules—one on the chest above the right breast and the other in the right axilla. These were excised. Histological examination of the excised grayish masses revealed that these were "plasmacytoma", metastatic from the nose and maxillary antrum. The previous biopsy slides were consequently reviewed and these two were truly "plasmacytoma". No therapy was given after excision. The BAT was still positive six months after the excision and by this time pain along the left ankle was noted by the patient. Radiological examination showed a suspicious involvement of the bones.

D. 1,000 mg dose:

Case 90: C.G., 39, female, underwent radical mastectomy of the right breast in July, 1958, followed by bilateral oophorectomy in September 1958. She was symptom-free for a year. After another year her urine became positive to the BAT but she was still symptomless. No therapy was given her. After six months she complained of back-aches. Her BAT had increased to +++. Radiological examination revealed metastatic involvement of the 9th and 10th ribs. She was placed on Thio-tepa therapy, receiving more than twenty-four injections. Because she had palpitation, weakness, and feeling of faintness after every injection therapy was discontinued. BAT was still positive. Radiological examination of the ribs did not show any change for the better. She was placed on Laetrile (nitriloside) therapy at a dose of 1,000 mg every other day. After a total of 41,000 mg, X-ray examinations showed the ribs were practically healed—the pains have gradually disappeared too. She is on a maintenance dose of 1,000 mg twice a month. Her urine is now negative with the BAT.

Case 91: A.B., 29, female, student nurse, underwent an open and close surgery for an abdominal tumor which turned out to be malignant, affecting both ovaries and involving the sigmoid. A piece of tissue was removed and this proved to be "schirrous cystadenocarcinoma". The patient underwent a course of Thio-tepa therapy for a total of 100 mg. After this treatment she still complained of pain on defecation, hypogastric pain, melena and cough; she lost five pounds. The BAT was +++. She was then started on Laetrile (nitriloside) therapy in December and by January she was back to work as operating room nurse. For four months she had only occasional twinges of pain; she regained the weight lost and the cough has completely disappeared. The lesion (?) in the right lung noted by radiography (when patient was still coughing) cleared up three months later. She received a total of 44,000 mg. When asked to evaluate her health, she claimed that in December it was only 50% normal; five months later it was 90%. Her urine is still positive with the BAT. She is on a 1,000 mg. dose every other day. Every now and then she receives the Laetrile (nitriloside) intravenously.

COMMENT

Laetrile (nitriloside) at the small dose of 100 mg administered by injection and iontophoresis has been effective par-

ticularly in early cases of metastasis (axilla) from operated breast cancer. The subsequent increase in the dose to 1,000 mg intravenously has effected more dramatic therapeutic results among the advanced cases of cancer as shown in the last two cases. The writer feels that the administration of Laetrile (nitriloside) in the 3,000-5,000 dose range would produce better anti-blastic effects.

CONCLUSION

The considerable increase in the therapeutic dose of Laetrile (nitriloside) produced more dramatic anti-blastic effects as compared to those achieved with the 50 mg dose used in 1952. These illustrative cases though few in number are sufficient to call to the attention of previous investigators, who claimed to have found Laetrile (nitriloside) useless at the smaller dose ranges suggesting that they try the drug again in the larger dose ranges.

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NITRILOSIDES (LAETRILES)

Their Rationale and Clinical Utilization in Human Cancer*

Ernst T. Krebs, Jr. and N. R. Bouziane, M.D., Ph.D.

INTRODUCTION

Some twenty years of research by Ernst T. Krebs, Jr., and associates of the John Beard Memorial Foundation in California have confirmed the suggestion of John Beard of Edinburgh University sixty years ago that the primitive trophoblast cell is the constant malignant component of all exhibitions of cancer. At least one chemical produced by this cell, human chorionic gonadotrophic hormone (HCGH), permits detection of cancer at a very early stage.

We have been using non-toxic nitrilosides (Laetrile), to which the trophoblast is susceptible, on terminal cancer cases for two years in Canada under the sponsorship of The McNaughton Foundation. Obviously, the nitrilosides (Laetries) would be better used prophylactically or therapeutically at a much earlier stage in the disease.

The results of this clinical evaluation will be presented following an outline of the scientific basis of this approach.

SCIENTIFIC BASIS OF THIS THERAPY

Effective, rational chemotherapy in human cancer depends ultimately upon whether this is biologically and biochemically a single disease or a multiplicity of diseases. As proponents of the Unitarian or Trophoblastic Thesis of Cancer¹ we believe that all established evidence supports the former. We maintain that the trophoblast cell is the constant malignant component not only of the malignant exhibition of cancer, chorionepithelioma, but also of all other exhibitions of cancer however morphologically it is masked; and that it is in every way identical with normal pregnancy trophoblast.

*December, 1962

It is another tenet of Beardianism that, just as the trophoblast of pregnancy is held in check first by the normally functioning maternal pancreas alone, and later by the fetal pancreas as well, the malignant induction of ectopic trophoblast likewise is prevented by the enzymatic processes of an intact pancreas. Should there be a deficiency, however, of pancreatic enzymes (be it genetic, infectious, degenerative, etc., origin) the uninhibited overgrowth of the placental or ectopic trophoblast results in hydatidiform mole or a chorionepithelioma, or in an exhibition of malignancy at the ectopic site as the case may be.

From theoretical consideration, then, the use of modified, more sensitive, micro-Aschheim Zondek tests^{2, 3} should demonstrate the presence of chorionic gonadotrophin^{4, 5} in the blood and urine of patients with chorionepitheliomas and much lower concentrations of this same cytотrophoblastic hormone in all other exhibitions of cancer—the concentration being proportional to the biological level of malignancy.⁶ These micro-Aschheim Zondek tests can also be used to evaluate the response of all types of cancer to chemotherapeutic agents.

Roffo's laboratory, Howard Beard, and Navarro and his colleagues at the University of Santo Tomas and the municipal hospitals of Manila have all reported 95-100% positive and negative accuracy in large series of cancer and non cancer patients respectively. They have all reported instances of subclinical detection of cancer or its recurrence prior to biopsy, cytology study or Roentrogram. Clinical investigators with Laetrile have reported cases in which consistently positive HCGH tests have become negative after parenteral administration. The amelioration of nonspecific signs and symptoms associated with positive reactors has accompanied many such instances.

BETA-GLUCURONIDASE

Independent of the foregoing considerations, Fishman⁷ in 1944 reported the presence of β -glucuronidase in malignant tissue. This enzyme, which hydrolyzes β -glucuronoside after the latter has been produced by oxidation of β -glucoside, was first reported to exist in animal tissue by Sera⁸ in 1914. Fishman and Anlyan^{9, 10, 11} have described levels of β -glucuronidase in surgically removed specimens of cancers of the breast, uterus, stomach and mesentery, abdominal wall, and esophagus 100 to 3600 times as high as levels of this enzyme in corresponding uninvolved tissue.

While they have empirically interpreted this as "a metabolic response of the tissue to estrogen or a related substance", Beardianism^{12, 13} maintains that this is directly related to the fact that the syncytial trophoblast produces abundant quantities of estrogenic and related steroids. These steroids elicit from the hostal tissue the production of β -glucuronidase necessary for their detoxification as the corresponding β -steroid glucuronosides, which are ultimately excreted in the urine as physiologically inert.

RHODANESE

In addition to their high levels of β -glucuronidase, malignant lesions are characterized by a generally profound deficiency of most other enzymes and a specific deficiency in rhodanese, as was reported by Homburger,¹⁴ and Mendel, Rodney and Bowman.¹⁵ Rosenthal reported an 80% decrease in rhodanese in hepatomatous liver tissue, and a similar decrease was found in the leukemic invasion of tissues.¹⁶

Lang,¹⁷ who discovered this enzyme in 1933, found that it converts hydrocyanic acid to rhodanate (thiocyanate or sulfocyanate) in the presence of thiosulfate or colloid sulfur thusly:



Sumner and Somers¹⁸ point out that rhodanese undoubtedly prevents the accumulation of excessively toxic exhibitions of HCN arising from the scission of dietary β -glucuronosides and β -glucosides by paralleling them both in sites of occurrence and in concentration. It exceeds the concentration of β -glucuronidase and B-glucosidase in all but malignant tissues. Whether or not human chorionic gonadotrophin produced by exhibitions of lesser malignancy accounts for the absence of rhodanese in the definitely malignant (trophoblast) cells, the fact that it does account for such rhodanese deficiency in the immediately contiguous somatic cells was demonstrated by Sanchez and Bertran.¹⁹ They reported that five international units of an aqueous solution of chorionic gonadotrophin 24 hours after injection decreased rhodanese activity in the tissues of rats 90% or more.

CYANOPHORIC GLUCOSIDES AND CYANOPHORIC GLUCURONOSIDES

Aware of the high concentration of β -glucuronidase in malignant tissue, Danielli²⁰ in 1950, and Conchie, Hay, and Levy²¹ and

Williams²² in 1961, suggested the use of glucuronides as tumor inhibiting agents. Working within the context of the unitarian or trophoblastic thesis of cancer, Krebs and others²³ as early as 1922 observed in crude vegetable extracts definitive palliative and therapeutic properties with respect to human cancer. In the 1940's he identified this property with such constituents of β -cyanogenetic glucosides as prunasin (1-mandelonitrile- β -glucoside) and amygdalin (d,L-mandelonitrile- β -gentiobioside). These materials were isolated in crystalline form and demonstrated to be non-toxic. Subsequent synthesis of specific glucuronosides such as 1-mandelonitrile- β -glucuronoside has provided preparations with therapeutic properties substantially superior to the previously demonstrated activity of the glucosidic nitrilonides.²⁴ A large homologous series of nitrilosides with widely varying aglycones and sugars is now under study.

PHARMACOLOGY AND TOXICOLOGY

When the Laetriles are incubated *in vitro* with a β -glucosidase there is a quantitative and dramatic release of HCN, nascent above its boiling point of 26°C. McIlroy²⁵ and Edmunds and Gunn²⁶ have demonstrated a clear counterpart to this reaction in both plants and animals.

The Laetriles are hydrolyzed *in vivo* to free nascent HCN, benzaldehyde, and a sugar or its acid. As previously explained the HCN is detoxified in somatic tissue by rhodanese to thiocyanate, which is then eliminated in the saliva, sweat, bile, and urine. The benzaldehyde is immediately oxidized to benzoic acid and detoxified through the liver by glycine conjugation as hippuric acid and/or glucuronic acid conjugation as benzoyl glucuronoside.

Since these nitrilosides are reasonably homologous with natural compounds found in many edible plants, and since all detoxification products are normal constituents of human blood and urine they are expectedly free of toxicity. The intact Laetile molecule is devoid of pharmacological or toxicological properties, these being present only after hydrolysis. Although free HCN is very volatile and may be lethal on inhalation, the cyanogenetic glucuronosides are non-toxic when administered parenterally. One gram of d,L-mandelonitrile- β -glucuronoside contains 30 mg of incipient HCN, and doses of over 5 grams have been administered intravenously without toxic effects. In normal tissues the excess of rhodanese, as compared with β -glucosidase and β -glucuronidase

results in the detoxification of scission products; but as the result of the lack of rhodanese in malignant cells, the HCN released by β -glucuronidase is not detoxified and remains free to exert its lethal effects against such cells and the contiguous somatic in which rhodanese is inhibited by chorionic gonadotrophin. Stern and Willheim²⁷ in their "Biochemistry of Malignant Tumors" have summarized evidence for the selective sensitivity of cancer cells to cyanides.

The present Laetriles depend for their cancericidal action almost exclusively upon potential HCN, although Waterman²⁸ has reported that benzaldehyde impedes the growth of inoculated tumors when brought into direct contact with the inoculum. Utilization of cancericidal aglycones and sugar derivatives will, of course, augment the present cancericidal action. While benzaldehyde and benzoic acid are, for example, antiseptic as well as analgesic, the substitution of an hydroxyl radical in the benzaldehyde ring would of course yield a more active analgesic upon hydrolysis—salicylic acid.

CLINICAL EVALUATION OF LAETRILE

Every chemical, reaction, product of reaction, source of reactants, and means of detoxification described above has been independently established and generally accepted. However, although the high concentration of β -glucuronidase, the apparent presence of a source of estrogen, and the deficiency of rhodanese have been empirically established in all exhibitions of cancer, acceptance of the above explanation of these phenomena in malignancies other than chorione epitheliomas is limited to adherents of the unitarian or trophoblastic thesis of cancer. We therefore feel that the Laetriles should be treated empirically as isolates in terms of ordinary clinical practicability until proof of their utility and the acceptance of that proof permits their return to this unified context of Beardianism.

The purpose of this clinical investigation was to determine whether there could be obtained at the malignant focus, a release of HCN of a magnitude sufficient to yield a substantial cytotoxic effect without exposing the host to undue toxicity. With the assistance of several medical associates a wide variety of terminal cancer cases, on whom all conventional methods of treatment had previously proved unsuccessful or inadvisable, were selected.

ADMINISTRATION

Laetrile is soluble in distilled water or normal salt solution and is administered parenterally. While some clinical investigators have given it intramuscularly, intrapleurally, intraperitoneally, locally, by means of arterial perfusion, and by iontophoresis, we have thus far used it only intravenously. Primary and secondary carcinomas of the lung have proved to be the most amenable to this route of therapy, because it avoids the rich reservoirs of β -glucuronidase in the liver, spleen, and kidneys. The most desirable route in malignancies beyond these organs can only be determined by an intelligent consideration of such factors as the underlying anatomy and physiopathology, the extent of the metastases, and the concentration of β -glucuronidase in the cells.

There has been considerable variation in the dosage of Laetrile administered. In the early 1950's Navarro²⁹ and others used 50-100 mg doses and in 1957 these were increased to 250-500 mg. The total dosage a patient received seldom exceeded 2 grams. We feel now that each patient should receive a minimum of 30 grams. In some cancers, such as carcinoma of the breast, and in instances when only a brief stay in hospital was possible, Laetrile was given in doses of 3 gms per day for 10 successive days. Other doctors have preferred to give 1 gm per day for 30 days.

It is our conclusion that, where time permits, it is most desirable to give the patient 1 gm of Laetrile every second day for the first 1-2 weeks. When it becomes evident that the drug is effective and that the patient is able to tolerate the breakdown of malignant tissue, this should be increased to 1 gm per day until the minimum dosage of 30 grams is attained. Such a routine produces results which are equally as good as those obtained with larger doses and seems to offer the advantage of taxing the regenerative processes of the body less severely.

In a few of the most terminal and hopeless cases death ensued before adequate treatment could be given. But most of the patients, having received the basic 30 grams of Laetrile and having then continued on a maintenance dosage of 1-2 grams per week, have become ambulatory and are gradually resuming their normal activities.

SUPPLEMENTARY THERAPY

It has been our experience that, while Laetrile alone has proved to be effective, even better results can be obtained with some sup-

plementary therapy as well. Pangamic acid is a methylating agent which appears to improve liver function with respect to its capacity to detoxify elements released from the malignant lesion following Laetrile therapy. Our patients received 100-200 mg of pangamic acid intramuscularly daily during their stay in hospital. Thereafter, a similar dosage was given with each maintenance dose of Laetrile. This substance may also be given orally should the patient so request it; but it appears to be more effective when given intramuscularly.

CRITERIA FOR EVALUATION

The progress of our patients was measured by a consideration of the clinical signs and symptoms, and by pathological, cytological, and radiological reports. Samples of the blood and urine were analyzed at intervals to detect any alterations in hematopoietic processes or in renal function during treatment.

RESULTS

Of the cases treated the results appearing in table 1 have been outlined because of the completeness of the data and because they serve to illustrate the wide range of malignancies which respond to Laetrile therapy. It is hoped that the following more detailed descriptions of some of the cases, might further illustrate our conclusions.

CASE #1:

Mr. A.G., 44 year old radio announcer, was perfectly well until May, 1960. When examined on June 7th he complained of dysphagia and otalgia of one month duration. Examination revealed a left anterior tonsillar pillar which was indurated, leukoplastic, and thickened at its inferior insertion. There was no evidence of adenopathy. A diagnosis of epidermoid carcinoma (Grade 1) was made on the basis of histopathological report following biopsy. Because of the radio-resistance of such lesions, the radiotherapy which had been initiated was discontinued and the patient was submitted to cobalt therapy during June, July and August. The lesion continued to progress and his general condition worsened; but, because of his occupation, he refused surgery. By March 20,

1961, cervical, brachial, and coronary adenopathy had developed to the extent that surgery was impossible. He had been able to swallow only liquids for six months.

On March 23, 1961, Laetrile therapy (1 gm per day I.V.) plus B15 (100 mg per day I.M.) was begun. After the first 6 grams of Laetrile progression of the lesion was halted and by April 4th he was released from hospital in a much improved condition. Dosage was reduced to 1 gm of Laetrile and 100 mg of B15 twice per week. By June 27, 1961, the dysphagia, adenopathy, and otalgia had disappeared, the primary lesion was considerably reduced in size, and the patient had gained 11 pounds.

During the last year, on a regimen of 1 gm. Laetrile and 100 mg of B15 one to two times per week, his condition has continued to improve and there is no longer any evidence of the primary lesion. With cessation of treatment with Laetrile for more than 6 weeks the dysphagia and otalgia return but there has been no recurrence of the primary lesion or of the cervical adenopathy. The patient will therefore continue on maintenance dosage indefinitely.

CASE #2:

Mrs. G.S., 63 year old housewife, was first diagnosed as having a glandular epithelioma of the left breast with metastases in November 1959. A radical mastectomy was performed at that time, and from Jan. 22 to April 4, 1960, she received radiotherapy (13,230 rads to the left axillary and supraclavicular regions, left chest, and mediastinum). On May 5, 1961, she was admitted to hospital completely incapacitated by pain and by intense dyspnea and severe coughing at the least effort. Physical and radiological examination revealed metastases to the right and left supraclavicular nodes and to both lungs—probably due to radiotherapy. Cytological reports on a left pleural effusion were negative. During her stay in hospital she received 200 mg of B15 intramuscularly each day and 1 gm of Laetrile intravenously every second day from May 24th until July 21st. From July 21st to July 28th she received 1 gm of Laetrile per day. Within a month after Laetrile therapy was begun her dyspnea and cough had disappeared and she had become ambulatory. When released from hospital on July 28, 1961, the patient appeared clinically to be greatly improved, although X-ray studies of the lungs showed no change with the exception of the absence of any pleural effusion.

Since that time she has continued to receive 1 gram of Laetrile I.V. and 200 mg of B15 I.M. twice weekly. Her pain has al-

most completely disappeared, she is no longer troubled by dyspnea or coughing, and she has gradually resumed her normal activities. It can be seen from the table that her blood picture has improved and there has been no evidence of any toxicity.

CASE #3:

Mrs. L.N., 52 year old housewife, was admitted to hospital March 6, 1962, with complaints of metrorrhagia of three months duration (menopause 6 years ago) and of right upper quadrant pain and dyspepsia of fifteen days duration. On the basis of clinical evidence and the cytological report following curettage a diagnosis of adenocarcinoma of the uterus (class V) was made. The patient was started on Laetrile on March 21, 1962, receiving intravenously 1 gm per day for three days and then 500 mg every second day, until her release from hospital on May 22nd. She was also given 100 mg of B15 every other day during hospitalization. A second cytological report on April 26th revealed no evidence of adenocarcinoma but only of endocervical hyperplasia. Her abdominal pain and metrorrhagia had ceased by this time and she had begun to gain weight. Since her release from hospital we have continued to give her 1 gm of Laetrile I.V. and 100 mg of B15 I.M. twice weekly. She has had no recurrence of symptoms, has regained her appetite and strength, is sleeping better, and does her housework without effort. Her urine, which originally contained traces of albumin and bacteria, mucus, hyalin casts and calcium oxylate crystals, is now normal. Her blood picture has not changed significantly, although Vita-Iron has been used to maintain her hemoglobin levels. No toxicity has been noted.

CASE #4:

This 55 year old patient, Mr. G.G., was admitted to hospital June 2, 1962. A barium series and cinefluorography at another hospital on May 7, 1962, had revealed an apithelioma of the esophagus. There was evidence of mucosal ulceration and of severe narrowing of the lumen for a length of 10 cm at the junction of the middle and lower thirds of the esophagus. At the time of admission to this hospital he was near death—unable to take any solid food and, in fact, even regurgitating liquids. He complained of pain in the right upper quadrant. X-rays of the lungs on June 4th revealed an ill-defined opacity in the right middle lobe sug-

gestive of pneumonia (he had been treated with tetracycline 2 weeks before for pneumonia), and pleural thickening and effusion on the left side. It was uncertain whether left pulmonary metastases were present. The patient was treated with Fortemycin and with 1 gram of Laetrile I.V. and 100 mg of B15 I.M. daily. He required Phenergan and Demerol in order to sleep at night. His pain fever had disappeared within 6 days, and after two weeks in hospital he was able to eat solid foods, had gained twelve pounds, and was ambulatory. X-rays of the lungs on June 16th were normal with the exception of some pleural thickening in the left axillary line. On June 24, 1962, the patient was released from hospital. Treatment was reduced to 1 gram of Laetrile I.V. and 100 mg of B15 I.M. every second day. X-ray studies of the lungs on July 27th were normal. A barium meal at this time revealed that the mucosa of an 8 cm segment of the distal third of the esophagus was irregular and that the lumen was somewhat reduced in calibre, but that the barium passed through without obstruction. The patient at present feels well and has returned to work. He no longer requires analgesics to sleep. His urine has been normal throughout the course of treatment; his hematocrit and hemoglobin, which were 31% and 10.2 gm% respectively on June 4th had increased to 37% and 11.8 gm% respectively by July 7th. There has been no evidence of toxicity.

CASE #5:

Mrs. G.M., 53 years old, was first discovered to have a glandular epithelioma of the ascending colon on August 20, 1961, at which time a resection and anastomosis was done. On Feb. 15, 1962, she presented with symptoms of obstruction. This was confirmed by barium enema and a second operation was performed on Feb. 20th. A recurrence of the glandular epithelioma was found at the site of anastomosis; this had spread to involve the posterior abdominal wall, a number of mesenteric lymph nodes and the greater omentum. It was impossible to excise the entire mass, but a side to side anastomosis of the terminal part of the ileum and the transverse colon was performed to relieve the obstruction.

She was then started on Laetrile, receiving 500 mg I.V. every second day for six days, then 1 gm per day for another six days. She has received 1 gm of Laetrile every second day since that time, and has also been given 200 mg of B15 I.M. with each injection of Laetrile. At present she is feeling very well and is ab-

to perform her household duties without difficulty. Her pain and colic is greatly diminished, her appetite has improved, her bowels are functioning normally, and she has no difficulty sleeping. There has been a noticeable reduction in the size of her abdominal mass. Urinalyses have remained normal and her hemoglobin, which had dropped to 10.6 gm% following her operation in February has increased to 11.7 gm%. There has been no indication of any toxicity.

CONCLUSION

To maintain that any of these patients has been cured—"cure" being defined as a five year period free of tumor recurrence—is not our purpose. In accordance with the concepts of Beardianism, cancer, like pellagra or scurvy, is a deficiency disease which must be controlled either permanently or until the enzymatic deficiency of the pancreas is rectified. It appears to us that the effectiveness of the Laetrile as such a palliative has been clearly demonstrated in a wide variety of malignant exhibitions, particularly in primary and secondary neoplasms of the lung.

It is also very evident that Laetrile possesses strong analgesic properties; and, although none of the patients mentioned in the above reports were troubled with fetor, in other cases treated this symptom was also relieved when present. Furthermore, there has been no indication of any toxicity in any of our cases in spite of the large amounts of Laetrile administered. In view of these facts it would seem only reasonable to suggest that this drug be more properly evaluated prior to the use of other palliatives, immediately following the detection of cancer.

It should be remembered, too, that to date the successful resolution of the anemias, vitamin deficiencies, and all other chronic diseases has only been accomplished by non-toxic physiologic means of prophylactic significance. Whether the systemically non-toxic and apparently cancericidal Laetries are also of preventative as well as palliative import is certainly worthy of additional scrutiny.

LEGEND

ABI - Ablated	Gland. Epith - Glandular Epithelioma	Inc - Increased	R - Reduced
Abn - Abnormal	N.A.C. - No appreciable change	AL - After Laetrile	NR - Not recorded
Ca - Carcinoma	R. H.W. - Resumed housework	BL - Before Laetrile	O - None present
S.R., - Slight reduction	R. W. - Resumed work	Imp. - Improved	N - Normal
Patient #1 - A.G.	#2 - G.S.	#3 - L.N.	#4 - G.G.
Age 44	63	52	55
Sex M	F	M	F
Diagnosis Epidermoid Ca. (grade 1) L. Ant. Tonsillar Pillar	Gland. Epith L. breast with metastases	Adeno Ca. of Esophagus	Gland. Epith Ascending colon
Method & Date of Diagnosis Biopsy 1-6-60	Biopsy	Cytology, Curetage 20-3-62	Barium Meal Cinefluorography 7-5-62
Treatment prior to Laetrile Radiotherapy cobalt therapy	Rad. Mastectomy 13-11-59 Radiotherapy (13,230)	None	Phenergan & Demerol
Laetrile Date begun Dose Frequency	22-3-61 1 gm 1-7 d	2-6-62 .5-1 gm 1-7 d	2-6-62 .5-1 gm 1-2 d
Approx. dosage to date	92 gms	236 gms	44 gms
Supplements	B15	B15	B15 Demerol Phenergan

ABI - Ablated

Abn - Abnormal

Ca - Carcinoma

S.R., - Slight reduction

Patient #1 - A.G.

Age 44

Sex M

Diagnosis Epidermoid Ca. (grade 1)
L. Ant. Tonsillar Pillar

Method & Date of Diagnosis Biopsy 1-6-60

Treatment prior to Laetrile Radiotherapy cobalt therapy

Laetrile
Date begun
Dose
Frequency

Approx. dosage to date

Supplements

Gland. Epith - Glandular Epithelioma

N.A.C. - No appreciable change

R. H.W. - Resumed housework

R. W. - Resumed work

Inc - Increased

No appreciable change

- Resumed housework

- Resumed work

AL - After Laetrile

BL - Before Laetrile

Imp. - Improved

R - Reduced

NR - Not recorded

O - None present

N - Normal

R.H.W. - Resumed housework

R.W. - Resumed work

Inc - Increased

No appreciable change

- Resumed housework

- Resumed work

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R - Reduced

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R. W. - Resumed work

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R. W. - Resumed work

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No appreciable change

- Resumed housework

- Resumed work

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BL - Before Laetrile

Imp. - Improved

R - Reduced

NR - Not recorded

O - None present

N - Normal

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- Resumed work

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BL - Before Laetrile

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AL - After Laetrile

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R - Reduced

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N.A.C. - No appreciable change

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R. W. - Resumed work

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- Resumed work

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BL - Before Laetrile

Imp. - Improved

R - Reduced

NR - Not recorded

O - None present

N - Normal

Gland. Epith - Glandular Epithelioma

N.A.C. - No appreciable change

R. H.W. - Resumed housework

R. W. - Resumed work

Inc - Increased

No appreciable change

- Resumed housework

- Resumed work

AL - After Laetrile

BL - Before Laetrile

Imp. - Improved

R - Reduced

NR - Not recorded

O - None present

N - Normal

Effect of

therapy upon:

Pain	Abl R	Abl Excised	R R	Abl R	R R
Tumor	Abl Inc.	Abl R-on diet	O O	O O	O O
Adenopathy	Abl Inc.		Inc. Inc.	Inc. Inc.	Inc. Inc.
Weight					
Appetite &					
Digestion	Imp. N	Imp. N	Imp. N	Imp. N	Imp. N
Bowels	O	O	O	O	O
Dyspnea	O	O	O	O	O
Cough	O	O	O	O	O
Dysphagia	Abl Inc.	Abl Inc.	O O	O O	O O
Activity	N	N	R. Hw.	R. Hw.	R. Hw.
Sleep			Imp.	Imp.	Imp.
Adverse effects	None	None	None	None	None
Urinalysis:					
Before	N	N	N	N	N
After	N	N	N	N	N
Hemogram:					
Date:	BL	10-5-61	7-3-62	4-8-62	18-2-62
Before RBC's	NP	3,700,000	NR	NR	3,990,000
WBC's	NP	12,400	14,400	10,500	8,550
Hb	NP	9.6 gm%	87%	12 gm%	10.8 gm%
Date:	12-6-62	3-3-62	30-5-62	7-7-62	19-7-62
After RBC's	4,600,000	4,700,000	NR	NR	3,900,000
WBC's	10,000	11,500	10,800	12,500	8,500
Hb	14.1 gm%	12.5 gm%	90%	71.8 gm%	11.7 gm%

Imp.

N

O

O

O

O

O

O

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O

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O

O

O

LEGEND

Abl - Ablated	Gland, Epith - Glandular Epithelioma	Ino - Increased	R - Reduced
Abn - Abnormal	N.A.C. - No appreciable change	AI - After Laetrile	N.R. - Not recorded
Ca - Carcinoma	R. Hw. - Resumed housework	BL - Before Laetrile	O - None present
Patient	#7 - D.D.*	#8 - A.F.	#10 - L.H.
Age	60	57	59
Sex	M	F	F
Diagnosis	Epithelioma of tongue	Ca. of Sigmoid with spread to adjacent nodes	Ca. of stomach Liver metastases
Method & Date of Diagnosis	Biopsy	Sigmoidoscopy Laparotomy Biopsy 1-12-61	Gastrectomy 1950
Treatment prior to Laetrile	Radiotherapy 24-4-61 to 12-7-61	Surgery 1-12-61	Cytology 3-5-61 25-5-61 (III-IV)
Laetrile	Date begun	17-8-61	10-5-61
Dose	1 gm 1-3 d	1 gm 1-4 d	1 gm 1-3 d
Frequency			1 gm 1-4 d
Approx. dosage to date	63 gms (12-1-61)	65 gms	168 gms
		80 gms	120 gm
			80 gms

* This patient was in excellent health, with no evidence of primary lesion when he stopped therapy (12-1-61). On 3-8-62 recurrence of primary lesion was noted and therapy resumed.
** Sites of osseous metastases have recalcified since initiation of therapy.

Supplements	B15	B15	B15	B15	B15
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Effect of therapy upon:

Pain	N.A.C.	Abn.	R	Abn.	Abn.
Tumor	Excised	R	O	R	R
Adenopathy	O	O	O	O	O
Weight	N.A.C.	N.A.C.	O	O	O
Appetite &		Inc.	O	Inc.	Inc.
Digestion	Imp.	Imp.	Imp.	Imp.	Imp.
Bowels	N	N	N	N	N
Dyspnea	O	O	O	O	O
Cough	O	O	O	O	O
Dysphagia	O	O	O	O	O
Activity	N.A.C.	R. H.W.	R. H.W.	R. W.	R. W.
Sleep	N.A.C.	N	N	N	N
Adverse effects	None	None	None	None	None
Urinalysis:					
Before	N	Abn.	N	NR	N
After	N	N	N	Abn.	N

Hemogram:

Date:	BL	BL	1-5-61	31-5-61	BL
Before RBC's	4,300,000	3,900,000	N	4,800,000	3,960,000
WBC's	9,100	14,700	6,800		
Hb	84%	10.1 gm%	12 gm%	12.35 gm%	12.4 gm%
Date:	AL	AL	6-6-62	6-6-62	10-5-62
After RBC's	4,280,000	4,000,000	4,400,000	4,300,000	4,800,000
WBC's	10,100	9,300	9,300	10,000	7,800
Hb	84%	12 gm%	13.5 gm%	14.3 gm%	12.4 gm%

SUMMARY

- 1) Malignant tumors are focally characterized by a high concentration of β -glucuronidase and a deficiency of rhodanese.
- 2) Specific nitrilosides (Laetriles), which upon hydrolysis yield hydrogen cyanide, an aglycone (benzaldehyde) and a sugar moiety, have been prepared to exploit this β -glucuronidase-rhodanese pattern.
- 3) Following parenteral administration there appears to be released in a wide variety of selectively sensitive malignant tissues such an excess of nascent HCN as to produce effects of definite palliative, and possible prophylactic, consequences in human cancer.
- 4) Laetrile also possesses strong analgesic properties and shows no evidence of any toxicity.
- 5) On the basis of the results reported in this paper and those obtained by other clinical investigators using Laetrile, it is suggested that this drug might be more properly evaluated in less terminal cases untreated by other palliatives.

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CHEMOTHERAPY OF INOPERABLE CANCER

Preliminary Report of 10 Cases

*Treated with Laetrile**
by

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The hope of the future lies in the chemotherapy of cancer. In view of deep-rooted prejudice against clinical experimentation in this field, a completely objective study and report of 10 cases should be of interest.

The use of Laetrile (1-mandelonitrile-beta-glucuronoside), a beta cyanogenetic glucoside, is based on the unitarian or trophoblastic thesis of cancer. In a review of 17,000 papers on malignant neoplasms and related biological subjects, the trophoblast was described as the *sine qua non* of cancer.¹

RATIONALE

The malignant lesion is characterized by a high focal concentration of beta-glucuronidase, which is a beta-glucosidase. Laetrile is a glucoside which is hydrolysed specifically by beta-glucosidase enzymes, with production of benzaldehyde, glucose, and nascent hydrogen cyanide.

Rhodanese, the cyanide-detoxifying enzyme, is absent or relatively deficient in malignant lesions but present in normal tissues. Nascent hydrocyanic acid is released to the extent of about 10% in the vulnerable carcinomatous areas but not elsewhere in the body.

Laetrile is relatively non-toxic when administered parenterally. Orally it is extremely toxic due to the release of hydrogen cyanide on contact with the hydrochloric acid of the gastric juice.

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LAETRILE: PREVIOUS REPORTS

In a group of 14 cases of cancer with metastases treated with Laetrile, there was striking relief of pain with discontinuance of analgesics, disappearance of fetor from ulceration, improved appetite and regression of the tumor.²

In another study of 21 terminal cases, the use of Laetrile provided satisfactory relief of pain, reduction of hemorrhage and jaundice, almost constant improvement in strength and the hematological pattern, and in some cases an appreciable reduction of the neoplastic mass.³

CLINICAL MATERIAL

The present group included 5 males and 5 females. The average age was 45, range 17 to 74. The diagnosis was adenocarcinoma of the breast 4 cases, Hodgkin's disease 3, cancer of the lung 1, cancer of the prostate 1, and cancer of the pancreas and omentum 1. Metastases were present in all cases.

Pain was a prominent symptom in all 10 cases and 7 patients required narcotics for relief.

Adenopathy was present in all cases and fetor in 1.

The average period of treatment with Laetrile was 17.5 weeks, range 4 to 43; average number of slow intravenous injections 30.2, range 6 to 79; average total dosage 46.2 Gm., range 9 to 133.

RESULTS OF TREATMENT

Dramatic relief of pain resulted in all 10 cases after the first or second slow intravenous injection and continued throughout the course of treatment. In 5 cases pain disappeared completely and in the other 5 it was definitely reduced. Narcotics were discontinued in 5 of the 7 cases in which they were used.

After 7 injections the fetor from an ulcerating adenocarcinoma of the breast disappeared and the discharge ceased.

Adenopathy was considerably reduced in 8 of the 10 cases in which it was present.

HEMOGRAM AND URINALYSIS

In all cases except #4 and #8, the blood picture was greatly improved after use of Laetrile. There was no indication of agranulocytosis or other hematogenous toxicity.

The average red blood cell count before treatment was 3,941,-000, after treatment 4,515,000 (15% increase). The average white blood cell count before treatment was 10,200, after treatment 9,750 (2% decrease, statistically insignificant). The average hemoglobin before treatment was 11.65 Gm. per 100 cc., after treatment 12.4 Gm. (6% increase). The before and after differential blood counts showed no significant changes and no abnormal blood cells were found.

Urinalysis was negative. Kidney function was not altered or affected by the use of Laetrile.

UNTOWARD REACTIONS

A sudden fall of blood pressure occurring five minutes after the injection was a common occurrence. In 1 case the drop amounted to 68 mm. and was accompanied by shock, requiring an injection of phenylephrine hydrochloride.

To avoid shock, I now use phenylephrine hydrochloride 0.3 mg. routinely in the same syringe with the Laetrile solution. This precaution has proved effective in maintaining a stable blood pressure during and after injections of Laetrile.

DISCUSSION

Laetrile is not a general analgesic *per se*, although on hydrolysis it releases a small amount of benzoic acid which is analgesic. Therefore the consistent relief of pain and discontinuance of narcotics after one or two injections, lasting throughout the course of treatment, are significant results. The sudden disappearance of fetor and discharge from ulcerating adenocarcinoma of the breast and reduction of adenopathy are also encouraging.

It would appear that Laetrile injections cause a regression of the malignant lesion. More cases and a follow-up study are required to evaluate the degree and permanence of this result. The findings present an image of cancer which is consistent with the trophoblastic thesis.⁴

CASE REPORTS

Case 1. W.L., age 62, female, married, housewife, weight 118 lb., height 62 in., blood pressure 144/95 mm. Diagnosis adenocarcinoma of both breasts with metastases to the skull, pelvis and spine. There was bilateral inguinal adenopathy. History of bilateral

mastectomy, eighteen years apart, followed by deep X-ray therapy. Urinalysis and hematology negative.

During the last six months the patient had suffered from constant excruciating pain in the back, entire spinal region, pelvis, thighs and legs. She was unable to lie down and tried to sleep in a chair. Repeated doses of codeine and other analgesics every two or three hours were required.

Laetrile 1 Gm. was injected intravenously. In five minutes the systolic blood pressure dropped 12 mm. but there were no other apparent effects. The following day the patient walked into my office without aid and reported that she had slept well with very little pain, that she needed less codeine, and that her appetite was good. Her general appearance was greatly improved.

An injection of Laetrile 1 Gm. was repeated. The systolic blood pressure fell 10 mm. but there were no apparent side effects. After ten minutes she said that pain was relieved completely and stepped down from the examining table without help.

In a period of one month she received six injections of Laetrile, four of 1 Gm. and two of 2 Gm. In each instance there was a prompt fall of blood pressure, average 10.4 mm., range 8-12 mm.

During the period of treatment the patient returned to her housework, was almost free from pain, discontinued codeine, took no analgesics other than 10 grains of aspirin at bedtime or during the night, and slept well. Her morale was excellent, her appetite good, and she gained 3½ lb. At the last examination she reported that she was completely free from pain. There were no apparent adverse effects from any of the injections. As of May 1, 1962 the hemogram showed distinct improvement in red blood cell count and hemoglobin, with no adverse change. Urinalysis was negative.

Case 2. J.S., age 74, male, married, pattern maker, weight 163 lb., height 62 in., blood pressure 188/100 mm. Diagnosis inoperable carcinoma of the left lung with metastasis to the mediastinum. Urinalysis and hematology negative.

During the last six months the patient complained of cough, constant chest pain, dyspnea, blood-tinged expectoration, anorexia, and loss of weight (15 lbs.). An X-ray revealed a mass in the left side of the chest suggestive of a neoplasm. Bronchoscopy and a biopsy established the diagnosis of carcinoma of the lung. Exploratory thoracotomy showed extensive carcinoma of the left lung with metastases and many perforations in the pleura, diaphragm, aorta, pericardium and mediastinum. The condition was considered inoperable.

Pain was so constant and severe that the patient took meperidine

hydrochloride and codeine every two or three hours. When interviewed, he had such great difficulty in talking and breathing that his wife had to give the history.

Physical examination revealed icteric sclerae, pallid conjunctivae, sluggish reflexes, enlarged and tender cervical and supraclavicular glands, dullness and moist rales over the left of the chest, and edema of the ankles extending up to the knees.

Laetrile 1 Gm. was injected intravenously. In five minutes the systolic blood pressure dropped 28 mm. but there were no signs of shock or other adverse effects. Three days later the patient reported that the pain had been less severe since the injection but that he had suffered for two days from pain in the left shoulder and side of the chest. Analgesics were still required.

After the second intravenous injection of Laetrile 1 Gm., the systolic blood pressure fell 15 mm. but there were no side effects other than burning and itching in the left shoulder area. One week later the patient returned to the office unassisted. Pain, dyspnea and edema were considerably diminished. His color and general appearance were considerably improved.

In a period of seven weeks he received sixteen injections of Laetrile, seven of 1 Gm., six of 1.5 Gm., and three of 2 Gm. There was a prompt fall of blood pressure following the injections, ranging from 8 to 28 mm. Pain was reduced and appetite improved but there was no weight gain. He was able to discontinue use of meperidine hydrochloride and codeine. There were no apparent adverse effects from the injections as shown by the before and after hemograms and urinalyses.

Case 3. J.C., age 40, female, married, housewife, weight 113 lb., height 61 in., blood pressure 140/90 mm. Diagnosis infiltrating carcinoma of the left breast invading the lymph nodes at all levels of the axilla, with metastases to the liver. Radical mastectomy and deep X-ray therapy. Urinalysis and hematology negative.

For the last six months she had suffered from very severe pain in the abdomen and back. Meperidine hydrochloride, morphine and opium were required for relief.

Laetrile 1 Gm. was injected intravenously. In five minutes the systolic blood pressure dropped 10 mm. but there were no other apparent effects. She returned the following day and reported no relief of pain.

An intravenous injection of Laetrile 1 Gm. was repeated, following which the systolic blood pressure dropped 12 mm. There was considerable reduction of pain and appetite improved after this injection.

In a period of four weeks she received twelve injections of Laetrile, ten of 1 Gm. and two of 1.5 Gm. Pain was relieved almost entirely and only a single dose of narcotic drug at bedtime was required. Morale and appetite were improved but there was no gain in weight. There were no apparent adverse effects from the injections. Comparison of before and after hemograms showed improvement in the red blood cell count and hemoglobin following Laetrile therapy.

Case 4. J.F., age 38, female, married housewife, weight 155 lb., height 62 in., blood pressure 160/90 mm. Diagnosis adenocarcinoma of left breast with carcinomatosis. Mastectomy, deep X-ray therapy and castration. Urinalysis and hematology negative.

The patient complained of agonizing pain in her spine, chest, pelvis, legs, arms and head. X-ray visualization confirmed the diagnosis of disseminated metastases. Adenopathy was present. Codeine, meperidine hydrochloride and opium were required to control the pain.

Laetrile 1 Gm. was injected intravenously. After fifteen minutes the systolic blood pressure rose 3 mm. There were no apparent side effects. On the following day pain was reduced, appetite improved, and the general condition was somewhat better.

A second intravenous injection of Laetrile 1 Gm. was given. In five minutes the systolic blood pressure dropped 16 mm. but there were no apparent side effects. Three days later the patient reported that the pain was considerably less and she required a minimum dosage of opiates for relief.

In a period of eighteen days she received eight injections of Laetrile, five of 1 Gm., two of 1.5 Gm. and 1 of 2 Gm. During the period of medication she showed progressive improvement and suffered very little pain. Opiates were no longer required. Morale was excellent. There were no apparent adverse effects from the injections. Comparison of before and after hemograms showed improvement in the red blood cell count and hemoglobin following Laetrile therapy.

Case 5. R.F., age 20, male, single, premedical student, weight 200 lb., height 59 in., blood pressure 114/70 mm. Diagnosis malignant lymphoma, type Hodgkin's. Condition started as enlarged cervical gland, diagnosis on biopsy. Urinalysis negative, hemoglobin 11 Gm./100 cc.

Deep X-ray therapy was employed. The patient complained of weakness, dizziness, and pain in the axillae and groin. The cervical

axillary and inguinal glands were palpably enlarged. The conjunctivae and sclerae were pale and icteric.

Laetrile 1 Gm. was injected intravenously. In ten minutes the systolic blood pressure dropped 6 mm. but there were no other apparent effects. Four days later the patient reported that he felt more active, had a better appetite, and had suffered no ill effects.

An injection of Laetrile 1 Gm. was repeated. The systolic blood pressure dropped 4 mm. in ten minutes, no other apparent effects.

In a period of four and a half months he received nineteen injections of Laetrile, five of 1 Gm. and fourteen of 2 Gm.

During the period of medication the pains in the neck and groin ceased and the adenopathy disappeared. The patient felt euphoric and his general appearance was considerably improved. There were no apparent adverse effects from the injections. The blood picture improved after Laetrile therapy.

Case 6. L.D., age 47, female, single, draftsman, weight 190 lb., height 66 in., blood pressure 280/110 mm. Diagnosis infiltrating adenocarcinoma of left breast. Both her mother and sister had died of cancer. History of radical mastectomy. Metastases in left axilla broke down, producing multiple sinuses.

The principal complaints were severe pain in the left side of the chest, necessitating the use of codeine, and a foul odor from the discharging sinuses. To control her distressing cough it was necessary to prescribe meperidine hydrochloride and opium for use on alternate days.

The left shoulder and arm were swollen and painful. The skin was glistening red. The circumference of the left mid-arm measured 19½ in. as compared with 13 in. for the right. Adenopathy was present in the entire left axillary and supraclavicular areas, both sides of the neck, and in the right breast. The liver was palpable and tender. Both sides of the chest were tender and especially painful on coughing.

Laetrile 1 Gm. was injected intravenously. In five minutes the systolic blood pressure dropped 38 mm. but there were no apparent other effects. On the following day she received a second injection. Pain and cough diminished and there was less discharge from the axillary sinuses. However, she felt a sense of heat and itching in the operative area. After the third injection pain was relieved completely and the fetor disappeared. After the fourth injection, the drainage ceased completely and the area was odorless. Multiple crusts covered the healing sinuses. Induration and inflammation were almost completely gone. The texture of the skin of the left arm had returned to normal.

In a period of five months she received fifty injections of Laetrile, nine of 1 Gm., thirty-nine of 2 Gm., and two of 2.5 Gm. The immediate hypotensive response was easily controlled when phenylephrine hydrochloride 0.3 mg. was used simultaneously with Laetrile.

During the period of treatment the patient returned to work. Pain and cough disappeared. The discharge from the metastatic sinuses ceased and there was no more fetor. The circumference of the left mid-arm was reduced from 19½ in. to 17 in., an indication of less tumefaction. Narcotics for relief of pain and cough were no longer required. There were no apparent adverse effects from any of the injections.

In this case treatment with Laetrile was continued from July 7, 1961 until May 1962. In the extended period of ten months the patient received 133 injections, twice a week or oftener. Comparison of before and after hemograms showed definite improvement in the red blood cell counts and hemoglobin. Adenopathy and tumefaction regressed to a considerable extent.

Case 7. G.P., age 21, male, single, college student, weight 149 lb., height 70 in., blood pressure 110/70 mm. Diagnosis malignant lymphoma, Hodgkin's type. Urinalysis and hematology negative.

A growing mass in front of the right ear, which returned four years after its initial appearance and recession, was removed and found to contain multinucleated giant cells typical of Hodgkin's disease. There was a hard, tender, enlarged lymph node in the mid-sternocleidomastoid region measuring 3x2 cm. Urinalysis and hematology were negative.

Laetrile 1 Gm. was injected intravenously. The systolic blood pressure dropped 4 mm. but there were no apparent side effects. Three days later the enlarged gland was smaller, softer, and less painful. By the sixth day all pain had ceased.

In a period of four months he received twenty-seven injections of Laetrile, ten of 1 Gm. and seventeen of 2 Gm. There were no side effects. One injection, made directly into the tumor mass, was followed by itching and local tenderness.

During the period of treatment the patient returned to college. Pain was absent, appetite good, weight increased 13 lb., and his appearance was excellent. The blood picture improved under Laetrile therapy.

Case 8. A.T., age 66, male, married, fireman, weight 120 lb., height 68 in., blood pressure 188/98 mm. Diagnosis inoperable

carcinoma of the prostate with possible metastasis to the liver. Hemoglobin 10 Gm./100 cc.

The patient complained of nocturia, hematuria, nausea, vomiting, and severe pain in the groin and thighs. Codeine and meperidine hydrochloride were required for relief. The skin and sclerae were jaundiced. There was painful adenopathy in both groins.

Laetrile 1 Gm. was injected intravenously. In seven minutes the blood pressure dropped 68 mm. and the skin became cold and clammy. The patient appeared to be in incipient shock but responded promptly to an injection of phenylephrine hydrochloride, after which his blood pressure recovered 66 mm.

Next day an injection of Laetrile 1 Gm. was repeated. His systolic blood pressure dropped 10 mm. but there was no shock reaction. Following the second injection the pain ceased and the use of narcotics was no longer needed. Nausea and vomiting were relieved, and jaundice was reduced.

In a period of four days he received three injections of Laetrile 1 Gm. During this time there was no pain and narcotic drugs were discontinued. Bleeding from the bladder ceased. Nausea and vomiting were relieved, and jaundice was diminished. Before and after hemograms and urinalyses showed no change.

Case 9. M.T., age 65, female, married, housewife, weight 110 lb., height 66 in., blood pressure 160/90 mm. Diagnosis adenocarcinoma of the pancreas and omentum. Hemoglobin 11.5 Gm./100 cc. The liver was palpable and painful nodules extended to about 3 inches below the costal margin.

During the last seven months she had suffered from extreme pain and had lost 20 lb. Meperidine hydrochloride was required for relief. She was exceedingly weak, jaundiced, emaciated, and unable to stand without assistance.

Laetrile 1 Gm. was injected intravenously. There were no adverse effects. A second injection was given four days later.

Pain was partially relieved and the dosage of meperidine hydrochloride was reduced. The blood picture and urinalysis showed no change under Laetrile therapy.

Case 10. F.E., age 17, male, single, student, weight 140 lb., height 71 in., blood pressure 110/70. Diagnosis Hodgkin's disease, granuloma type, with metastasis to the thorax.

During the last three months a growing mass in the left supraclavicular region had reached the size of a quarter sphere of an average orange. The patient complained of pain in both axillae, weakness, nausea and anorexia. He had lost 25 lb. and was jaun-

diced. Biopsy confirmed the diagnosis. The axillary lymph glands were enlarged, especially on the right side. The roentgenograms showed progressive nodal enlargement inside the thorax.

Laetrile 1 Gm. was injected intravenously. In five minutes the systolic blood pressure dropped 6 mm. but there were no apparent other effects.

On examination two days later the mass in the neck was softer and smaller. By the fifth day it was reduced to about half the original size, and was softer and movable. The axillary lymph glands were barely palpable. He was free from pain and his appetite had returned.

In a period of five months he received thirty-six injections of Laetrile, nineteen of 1 Gm. and seventeen of 2 Gm. There were no side effects.

During the period of treatment there was no pain and no enlargement of the supraclavicular mass occurred. Appetite improved and the patient gained 24 lb. He returned to his studies. Comparison of before and after hemograms showed distinct improvement in the red blood cell count and hemoglobin.

SUMMARY

The use of Laetrile (1-mandelonitrile-beta-glucuronoside), a beta cyanogenetic glucoside, intravenously in 10 cases of inoperable cancer, all with metastases, provided dramatic relief of pain, discontinuance of narcotics, control of fetor, improved appetite, and reduction of adenopathy. The results suggest regression of the malignant lesion.

A fall of blood pressure occurred in all cases after administration of Laetrile. This side effect was easily avoided by using phenylephrine hydrochloride 0.3-1 mg. in the same syringe with the Laetrile solution.

No other side effects were noted except slight itching and a sensation of heat in the affected areas, which was transitory in all cases.

Comparison of before and after hemograms showed definite improvement in the red blood cell count and hemoglobin in most cases. Differential blood counts and urinalyses were entirely negative.

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QUESTIONS & ANSWERS RELATING TO THE UNITARIAN OR TROPHOBLASTIC THESIS OF CANCER

by Ernst T. Krebs, Jr.

- Q.** Are cigarettes carcinogenic, and if so how can we account for their carcinogenicity in the light of the unitarian or trophoblastic thesis of cancer?

A. The evidence for the carcinogenicity of cigarettes is now overwhelming, and we believe that any attempt to ignore this evidence a manifestation of an anti-intellectual or anti-scientific attitude probably arising from the wishful thinking of inveterate smokers. The American Cancer Society, the United States Public Health Service, and a number of medical societies have formally declared themselves against the use of cigarettes on these grounds.

So far as the Beardian thesis is concerned, the sequence of cigarette carcinogenicity runs something like this: (1) the tars and heat set up a low grade inflammation, (2) the afferent vessels in the inflammatory area tend to develop fibrin plugs which result in the selective localization of cigarette tars, (3) the cigarette tars contain such carcinogens as benzpyrene, (4) benzyprene is estrogenic (it produces cornification in the vaginal tract of immature female mice), (5) the estrogenic effect provides a congenial decidua for the growth of the estopic trophoblast that arises consequent to the division of the haploid gametogenous cell arising through such meiosis, and (6) the presence of the trophoblast elicits beta-glucuronidase from the contiguous somatic cells and depresses all rhodanese activity.

- Q.** I have heard that some clinicians claim that the palliative action of Laetrile is more apparent in lung cancer than in any

other exhibition of cancer. Is this true and how does it square with the claim that all exhibitions of cancer have trophoblast as a constant malignant component?

A. All exhibitions of cancer do have trophoblast as a constant malignant component and if drugs that act against this component could be brought in equal quantities to this component wherever it is found, the palliative responses would be equal. But in many exhibitions of cancer the anatomical situation is such that a large bulk of the laetrile is adventitiously hydrolyzed (with HCN scission) by the beta-glucuronidase-rhodanese reservoirs normally contained in the liver, spleen, and kidneys.

In the case of pulmonary cancer an intravenous injection of Laetrile is carried directly to the right heart, bypassing the liver and the spleen and the kidneys, and from the right heart it is carried directly to the lungs *before* any adventitious scission of the molecule occurs. This is why both primary and secondary growths here usually show a superior palliative response.

3. Q. Are we to conclude from your statement that since the unitarian or trophoblastic thesis of cancer will admit of no logical alternative that the vast body of knowledge we now possess on cancer is invalid?

A. No; the unitarian or trophoblastic thesis is the only explanation of cancer that gives this vast body of knowledge illumination or rationality. Of the thousands of papers appearing in the first rate medical or scientific journals we have found that over 98 per cent of them are not only wholly congruent with the Beardian thesis but that in this explanation alone most of them find rational and scientific justification.

4. Q. Didn't you invent the use of chymotrypsin and, I think, trypsin in the treatment of human cancer before you came up with Laetrile?

A. Let's first clarify our terms. Invention is one thing; discovery is another; and development is another. If the pancreatic antithesis to trophoblast or its homologues or to cancer

was "invented," it was "invented" through the blind forces of natural selection working over aeons of time. I did *discover* the relevance of crystalline chymotrypsin to the selective destruction of trophoblastic or cancer proteins. I then *developed* its application in the palliation of mammalian cancer.

5. Q. But weren't your discoveries on the parenteral use of trypsin, chymotrypsin and the other crystalline pancreatic enzymes thoroughly discredited?

A. Both parenteral chymotrypsin and trypsin are now used routinely in almost every hospital in the world. They are used to control pain, inflammation and edema. As you know, pain, inflammation and edema sometimes occur in cancer. When they do, these agents control such pain, inflammation and edema just as they do in non-cancerous patients. Let me read you a note published from two universities in 1949. The authors described parenteral chymotrypsin as so dangerous as to be a hazard to human life. The same chymotrypsin in the same doses is now used to correct in a non-toxic fashion the allegedly terrible toxicities once ascribed to these two enzymes.

6. Q. But wasn't it actually Northrop and Kunitz of the Rockefeller Institute who first obtained these enzymes in crystalline form?

A. That is true. In the '40's the Rockefeller Institute had so little chymotrypsin that they asked the John Beard Memorial Foundation to supply them with some, which we did.

7. Q. But didn't you originally claim that the pancreatic enzymes parenterally used were useful specifically in mammalian cancer?

A. Yes; I have not changed—or the reality has not changed. First no one would look at these enzymes medically—they were damned. We insisted they had value. Then they were tentatively accepted. Then they were accepted for the control of pain, inflammation and edema. Then they found acceptable application in the digestion of hematomas. There are now papers on their use in the dissolution of intravascular blood

clots. . . . I am optimistic enough to recognize that evolution is not going to stop here. The crystalline pancreatic enzymes will inevitably come into universal use in the control of cancer.

Let's keep in mind one fact. Trypsin and chymotrypsin parenterally administered are, so far as we know, the only therapeutically successful byproducts of research in cancer. Consider that over two billion dollars has been spent in this country for modern cancer research and that the only group that produced two universally recognized contributions is a Foundation that did not spend one cent of this two billion.

8. Q. But what evidence do you have that the pancreatic enzymes destroy human trophoblast—I go along with the unitarian or trophoblastic thesis, since we all know it can't be disproved?

A. There are many pieces of evidence for this. Let's take the most commonplace one—something universally taught medical students commencing with their biochemistry and extending to their course in obstetrics. Mothers with diabetes mellitus are obviously suffering from a pancreatic deficiency in endocrine function. As numerous workers have shown, such an endocrine deficiency is usually accompanied by a corresponding exocrine deficiency—a deficiency in the production of pancreatic enzymes.

In women who are diabetic there is a marked overgrowth of pregnancy trophoblast as a result of pancreatic failure. This overgrowth is reflected in a strikingly high elevation in the chorionic gonadotrophin titer of the blood and serum. The administration of insulin does not correct this process. The overgrowth of the trophoblast is accompanied by a degree of pregnancy toxemia, which tends to vary in severity directly with the blood and urine titer of chorionic gonadotrophin. (Most of the references for all this are given in the Krebs and Bartlett 1949 paper on pregnancy toxemias, which incidentally is cited four times in Dieckmann's classical volume on the pregnancy toxemias.) You see, pregnancy trophoblast overgrows in the presence of a non-insulin pancreatic failure. In women not yet diabetic but who subsequently become diabetic there is a history of a very high incidence of pregnancy toxemias.

9. Q. If the pancreatic enzymes destroy trophoblast so efficiently, why aren't they more widely used in human cancer?

A. The evolution of their clinical use has been a long and painful one. It was first limited by the unavailability of active preparations and the extreme toxicity of crude pancreatin preparations. Despite this, excellent physicians more than half a century ago published reports of the clinical effectiveness of crude pancreas extract in human cancer—some publications in the Journals of the American Medical Association and the British Medical Association. In the 1940's, our Foundation first made crystalline chymotrypsin available. It definitely produced substantial palliative effects in human cancer. Others reported effects from crystalline trypsin. Others from a combination of the two enzymes. As late as 1954 Ledoux, and in 1957, Pileri et al., showed that *in vitro* suspensions of Ehrlich and Landschutz tumor ascites cells were destroyed by pancreatic ribonuclease. Survival time was increased with this enzyme in the case of Walker carcinome 256 in ascites form. Spontaneous mammary tumors responded with a temporary arrest in growth. Bergel and Smith confirmed these observations. A review is presented in "Chemistry of Enzymes in Cancer" by Franz Bergel, Charles C. Thomas, Springfield, 1961.

Crystalline pancreatic chymotrypsin, trypsin, ribonuclease, deoxyribonuclease, and carboxypeptidase have all shown selective activity against trophoblast, animal cancer, and human cancer. Pancreatic deoxyribonuclease or dornase has, of course, come into almost universal use in the debridement of wounds. (e.g., Parke-Davis' Elastase).

10. Q. But all this does not *prove* the utility of crystalline pancreatic enzymes in human cancer, despite the fact that you can say that chymotrypsin and trypsin are now used to relieve pain, inflammation and edema *wherever* found and that deoxyribonuclease is used in debriding wounds. Such use in cancer isn't what you originally meant.

A. Not exclusively what we originally meant nor what John Beard originally meant when on embryological grounds he urged the use of *all* pancreatic enzymes in human cancer. . . . We do not want to explore the controversial area of clinical

application here, but I can cite as a matter of fact the case of one Carl King who was urged to have an amputation of his right arm by several hospital tumor boards in Los Angeles. This man instead went to Dayton, Ohio to be treated by a prominent surgeon who experimentally uses a parenteral combination of trypsin, chymotrypsin, ribonuclease, deoxyribonuclease and carboxypeptidase in human cancer. A complete recovery of now over four years duration was achieved. The laboratory and clinical protocols of this case are available upon request as is the name of the surgeon, who is an excellent Beardian but not affiliated with any Beardian organization.

11. Q. Then you believe that the crystalline pancreatic enzymes will ultimately come into their own in destroying cancer or trophoblast?

A. They are already in their own so far as destroying trophoblast. We would not be talking to each other had not the pancreatic enzymes destroyed our gestational trophoblast. Had they not done this we would have terminated our genetic patterns in a spontaneous abortion, a hydatid mole, or a fulminating primary uterine chorionepithelioma. You know, mankind had breathed an ocean of oxygen long before Lavoisier got around to discovering it. Let's hope that mankind will not have to leave the pancreatic enzymes remain much longer as relatively undiscovered destroyers of trophoblast—especially the trophoblast of cancer.

12. Q. Where does all this leave the laetriles?

A. It leaves them playing their indispensable roles in animal physiology and pathology. They represent the exogenous means by which trophoblast may be destroyed; the crystalline pancreatic enzymes represent the endogenous means.

13. Q. You discovered the laetriles then, rather than invented them?

A. Yes; without them none of us would be here. We could not live without hemoglobin—or the hematin molecule. We

could not have hemoglobin without vitamin B₁₂—another name for vitamin B₁₂ is cyanocobalamin. *Cyano* means the same thing as *nitrile*. The precursor to cyanocobalamin is hydrocobalamin. The latter gets its labile nitrile group from laetries that are ingested in the diet. Either directly through eating lima beans, apples (seeds, too), peaches, etc., or through eating the meat of animals who have taken their laetries from clovers, Johnson grass, etc. In other words, almost all the thiocyanate we carry in our blood, saliva, urine, tears, arose directly or indirectly from ingested laetries.

Studies with radio-active tracers show that the nitrilization of hydrocobalamin to cyanocobalamin occurs through the thiocyanates that have arisen as the result of the hydrolysis of beta cyanogenetic glucosides and glucuronidases by tissue beta-glucosidases and beta-glucuronidases and the subsequent detoxification of the HCN by rhodanese to the corresponding thiocyanate.

14. Q. What would happen if a cell possessed beta-glucuronidase but lacked the enzyme rhodanese?

A. The cell would be unable to protect itself from the nascent cyanide and would, therefore, be destroyed.

Before we get into the laetries and human cancer, let's make this clear. The laetries are a part of our universe; they are here to stay—just like chymotrypsin, trypsin, deoxyribonuclease, etc. To treat them as anything but such a reality is stupid, and reflects nothing more than an inadequate knowledge of certain phases of physiology and biochemistry.

The John Beard Memorial Foundation was, so far as we know, the first organization to make a systematic scientific and clinical study of these indispensable factors in normal animal metabolism. Let's get this clear: without laetries there would be no life.

15. Q. Is that an exaggeration?

A. Have you tried to live without hemoglobin or tried to make cyanocobalamin from un-nitrilized hydrocobalamin? Without beta cyanogenetic glucosides there would be no life. We can

live very well without nitrogen mustards, H-bombs or even cobalt bombs. We can't live without laetriles.

16. Q. How is it that both the pancreatic enzymes and the laetriles are completely non-toxic, but that all other forms of cancer chemotherapy—at least the accepted forms—are extremely toxic?

A. Cancer is one of the chronic diseases. It is axiomatic—though we too seldom ponder the fact—that no chronic disease has ever been conquered except by utterly non-toxic means. The more non-toxic the means, the more certain the therapy. Nor do we seriously hope to conquer any chronic disease except by non-toxic means. What are the best biochemical hopes in cardiovascular diseases, for example. Pellagra, beriberi, scurvy, rickets, pernicious anemia, etc.—without exception their conquest has been through non-toxic means. Why should cancer prove an exception?

17. Q. Don't the nitrogen mustards, the antimetabolites, Velban, Methotrexate and the rest do some good in cancer?

A. This is a medical or clinical question. Some good, under certain conditions, may be temporarily achieved by destroying an excess of normal somatic cells, especially if among them are some trophoblast cells. But such destruction is directed biologically not against definitively malignant cells but against somatic cells.

For example, most of the toxic drugs mentioned have some value in leukemias. But if one ingests or injects such drugs in a normal individual, these drugs will cause a profound decrease in the white blood count. When trophoblast occurs in myelogenous and lymphatic tissues, the resultant leukemic exhibition will comprise an abundance of primitive somatic myelocytes or lymphocytes. If one uses something that will destroy normal white blood cells, the excess of white blood cells will be destroyed and the WBC count will fall. It might even fall to normal. This means only that the reactive somatic cells have been destroyed. For all practical purposes the definitively malignant cells have not been touched. Sometimes the removal of excess quantities of such somatic cells does

provide temporary comfort or palliation, but it is important to bear in mind just what is happening and just what is being destroyed: normal somatic, not cancer cells.

18. Q. Do you mean that the constant malignant component—as you call it—is trophoblast even in the leukemias?

A. Yes.

19. Q. What proof do you have for this?

A. We can cite at least fifty instances from the literature of pathology in which primary exhibitions of trophoblast in chorionepitheliomatous exhibitions have metastasized to be exhibited as adenocarcinomatous exhibitions; or we can cite instances in which the latter as primary growths have exhibited frank trophoblast in a secondary chorionepitheliomatous exhibition. We can also cite instances in which an exhibition has graded by imperceptible degrees into an adenocarcinomatous exhibition. There are other examples in which adenocarcinomatous exhibitions have produced extremely high titers of chorionic gonadotrophin.

20. Q. Since cancer is trophoblast and trophoblast is the most primitive embryonic cell in the life-cycle and the most undifferentiated cell in the life-cycle, why then doesn't the so-called constant malignant component in all exhibitions of cancer selectively yield to the destructive action of radiation?

A. It is, first of all, imperative to bear always in mind that the trophoblast cell is *not* an embryonic cell. It exists before the definitive embryo and neither forms the definitive embryo nor can it be formed by the definitive embryo. Moreover it is, despite being the most primitive cell in the life-cycle, a completely differentiated cell in the same sense that a functioning neuron is a completely differentiated cell. As tissue culture and other studies have shown, the trophoblast is in extreme or fierce antithesis to *every* somatic or definitive body cell in the life-cycle.

The Law of Bergonie et Tribondeau is a valid, an excellent, generalization that is applicable to *all* somatic body cells. It applies, for example, to primitive blood cells, connective tissue cells, glandular tissue, etc. A primitive neuroblast, for example, is highly radio-sensitive; a functional neuron is highly radio-resistant. Primitive fibroblasts are radio-sensitive; cartilage and bone are radio-resistant. The embryonic (*not* extra-embryonic) blastoderm is extremely radio-sensitive; trophoblast is extremely radio-resistant.

21. Q. What experimental proof is there for the radio-resistance of trophoblast?

A. Trophoblast cells in normal pregnancy withstand successfully enormous doses of radiation without any appreciable depression in growth, as measured physically and by chorionic gonadotrophin excretion. Of course, the radio-resistance of primary uterine chorionepitheliomas is classical. The latter exhibition indicates to us the basis for the selective radio-resistance of cancer cells. Chorionepithelioma, comprised of pure trophoblast indistinguishable cytologically or endocrinologically from pregnancy trophoblast, is the most malignant of all exhibitions of cancer. If the definitively malignant cells were selectively susceptible to radiation, chorionepitheliomas would be the most radio-sensitive of all growths, not the most radio-resistant.

22. Q. You have often described the chorionepitheliomas—comprised of pure trophoblast—as the most malignant of exhibitions of cancer. Isn't it true that the malignant melanomata are just about as malignant as chorionepitheliomas; yet they show no frank trophoblast?

A. Malignant melanomata comprise a composite of melanoblasts, melanocytes and trophoblast. In tissue culture, a number of observers report, that there is a dissociation between the melanoblasts and melanocytes, on the one hand, and what they call "the definitively malignant cells", on the other. This dissociation may also occur clinically in the case of the so-called unpigmented melanomata.

Melanocytes are, of course, somatic or benign body cells;

but they possess the extraordinary property of physiological metastases or migration. Benign melanocytes are capable of migrating throughout the body to form benign melantomatos growths. Now, combine this unique property of active migration possessed by the melanocytes with the highly metastatic properties of normal trophoblast in a malignant melanoma and you have an extremely malignant process because the trophoblastic capacity of metastases is added to the unique somatic capacity of migration possessed by the definitive melanoblasts or melanocytes.

23. Q. Why doesn't the trophoblast go ahead and differentiate into definitive embryonic tissue?
- A. For the same reason that cancer does not differentiate into benign tissue. Trophoblast represents the end of a morphogenetic line.
24. Q. How does the definitive embryo form, then, in normal gestation?
- A. The so-called embryo-forming cells—diploid totipotent cells—are segregated from the trophoblast cells (asexual) generation by the fourth cleavage stage. From thence on the one can not become the other. One of these diploid totipotent cells goes to form the definitive embryo (sexual generation) within the trophoblastic blastocyst while the remaining diploid totipotent cells migrate into the definitive embryo where about 80 per cent of them reach the area of the future gonads. The products of their geometric division become, as development proceeds, very great.
25. Q. What happens to the diploid totipotent cells that reach the gonads?
- A. In time they undergo meiosis to form haploid gametogenous cells—cells with half the normal chromosome complement. Upon division these cells produce trophoblast. They may be induced to division normally through fertilization, during which the diploid number is restored, or they may be induced

to division by non-sexual means in either the male or the female. At any rate, the first cell formed is trophoblast of a genetic constitution unique from that of the host.

26. Q. What causes the diploid totipotent cells in the gonads to undergo meiosis to form haploid gametogenous cells?

A. A sex steroid hormone known generically as estrogen. It is what we in biochemical morphogenesis call an *inductor* or *organizer* compound.

27. Q. What happens if one of the diploid totipotent cells that reside among the various multipotent cells of the soma undergo meiosis with the division of the consequent gametogenous cell?

A. Trophoblast or cancer is formed.

28. Q. Why do you say "trophoblast or cancer"? Why can't trophoblast of a non-cancerous nature be formed?

A. Let's recall one fact: in the whole history of medicine no one has ever seen a trophoblast cell multiplying in a male or non-pregnant female except as cancer; nor has one ever so seen the hormone of trophoblast—chorionic gonadotrophin.

29. Q. What happens if estrogen impinges on a diploid totipotent cell in the breast or stomach, for example?

A. Cancer of the breast or stomach is the morphogenetic exhibition that results.

30. Q. Is estrogen "carcinogenic"?

A. Many writers have emphasized the commonplace fact that estrogen is the *only* carcinogen normally and regularly found in the animal body. We do not like to call estrogen or any

other similar substance a "carcinogen." We prefer the terms "inductor" or "organizer."

31. Q. Why is estrogen the only normally occurring carcinogen discovered to date in the animal body?

A. Because estrogen is the only known normally-occurring substance that induces meiosis of diploid totipotent cells by which haploid gametogenous cells that produce trophoblast on division are formed.

32. Q. Isn't the explanation of the carcinogenicity of estrogen that you give an after-thought or a rationalization?

A. In 1902 John Beard on embryological grounds discovered that cancer is trophoblast (asexual generation). The estrogens were not even discovered at Beard's death in 1924. But because cancer is trophoblast and trophoblast is normally brought into being through estrogen, Beardians knew that estrogen must be the *only* normally occurring so-called carcinogen. Think of the probability of this single correlation being a matter of chance or accident.

33. Q. How does the organism normally protect itself from the excessive action of estrogen?

A. Through an enzyme known as *beta-glucuronidase*. This enzyme conjugates a molecule of estrogen with a molecule of glucuronic acid to form an estrogen beta-glucuronoside which is excreted through the urine as a virtually non-toxic compound.

34. Q. Why does trophoblast morphologically mask itself or induce the proliferation of so much somatic or hostal tissue, as you call it?

A. The syncytial aspect of trophoblast produces at least three common steroid hormones: estrogens, progesterones, and cor-

tisone. We know the morphogenetic effects of estrogen, for example, on mammary glands, uterine tissue, the skeletal system and the lymphoid tissue. In all estrogen induces both hyperplastic and hypertropic changes, it causes the differentiation of functional glandular tissue, etc. That is just one of the syncytial steroids of the trophoblast. Multiply these effects by the remainder of these steroids.

35. Q. You often speak of the enzyme beta-glucuronidase as focal-ly characterizing the malignant lesion. Did you discover this?

A. No; the focal characterization of malignant lesions by high concentrations of beta-glucuronidase is a phenomenon discovered by Levvy, I believe, in England, and independently by Fishman in the United States. Dozens of workers have confirmed this scientific commonplace.

36. Q. Don't these workers know that estrogenic steroids are also present in the malignant lesion?

A. Yes; most of these workers have concluded that. They are, of course, utterly mystified as to how the estrogen gets there and why, after it gets there, a specific enzyme mechanism for its detoxification should be awaiting it.

37. Q. Do they reject the unitarian or trophoblastic thesis of cancer?

A. No one rejects the unitarian or trophoblastic fact of cancer. Some are not aware of it and others do not understand it, but to reject it would require saying, in effect, "cancer is not trophoblastic or an unitarian phenomenon *because . . .*" That *because* has, of course, precluded anyone's rejecting the trophoblastic fact.

Bear in mind that as our knowledge increases, the old ideas of the basic multiplicity of malignant exhibitions, the spontaneous generation of cancer cells, etc. become increasingly preposterous. In addition to postulating the spontaneous generation of cancer cells one would be faced by the necessity of postulating their accidental production of estrogen, the acci-

dental capacity of the organism to supply a specific enzyme to detoxify the estrogen-beta-glucuronidase, etc. Such elaborate mechanisms are the products of natural selection working over aeons of time in response to unfolding needs.

38. Q. Why do you give "spontaneous generation" as the only alternative to the trophoblastic nature of cancer?

A. A pathological cell either has its normal counterpart in the life-cycle or it does not have its normal counterpart in the life-cycle. The cancer cell is either a cell with a counterpart in the life-cycle or one without a counterpart in the life-cycle; hence a spontaneously generated cell.

39. Q. That is obvious, but why choose the trophoblast cell?

A. It is the most primitive cell in the life-cycle and possesses every attribute of the cancer cell and lacks no attribute possessed by the cancer cell. No other cell in the life-cycle vaguely resembles the trophoblast cell.

40. Q. You ascribe cancer to the non-sexual activation of a haploid cell, but suppose the haploid cell is normally fertilized?

A. Cancer is trophoblast. It makes no difference whether this trophoblast comes into being as a result of fertilization or non-sexual enactivation. In fact, the trophoblast of one of the most malignant exhibitions of cancer—primary uterine chorion-epithelioma—arises from the simple proliferation of trophoblast that has come into being as a result of normal sexual fertilization.

On the other hand, the trophoblast of primary testicular chorionepithelioma comes into being as the result of the non-sexual activation of a haploid gametogenous cell, yet the trophoblast of the two sources are endocrinologically and cytologically and otherwise indistinguishable.

41. Q. Would you call the described growths *neoplasms*?

A. According to the unitarian or trophoblastic thesis of cancer, not *all* neoplasms are malignant—almost all, but not all. The only major non-malignant neoplasm is the ovarian dermoid cyst. The embryonic phase of a testicular chorioneopthelioma is also neoplastic and basically benign but since it is almost invariably infiltrated by the contiguous trophoblast it is called cancerous or malignant.

42. Q. What determines true neoplasia according to your definition?

A. A neoplasm is a growth the cells of which are of a genetic constitution foreign to that of the host.

43. Q. A foetus is by your definition a neoplasm, then?

A. Yes.

44. Q. The trophoblast, too?

A. Yes. It is a malignant neoplasm; the embryo or non-trophoblast is a benign neoplasm.

45. Q. A primary uterine chorioneopthelioma is a neoplasm, then?

A. Yes.

46. Q. The trophoblast from the placenta that congenitally lodges in the retina to form a highly malignant retinoblastoma is then not actually a neoplasm since it belongs to the same genetic constitution as the host?

A. That is correct. This unique tumor is probably the only form of cancer—if we exclude blood moles—that is not neoplastic. This is slicing it rather thin, but you can do that in an exact science.

47. Q. Will the pancreatic enzymes act against any of the benign growths?

A. Definitely not.

48. Q. Will the laetriles act against them?

A. No.

49. Q. Why not? Levvy and others point out that rapidly multiplying primitive somatic cells are rich in beta-glucuronidase.

A. That is true but the beta-glucuronidase in these cells is accompanied by a physiological excess of the enzyme rhodanese—an excess beyond that required for the full detoxification as thiocyanates of *any* HCN that might be liberated from the laetriles.

50. Q. Incidentally, why do these benign or somatic cells during rapid proliferation show such high levels of beta-glucuronidase when there are no syncytial trophoblast elements presented to supply estrogen or similar steroids?

A. You will recall that we described estrogen as an *organizer* or *inductor*. Organizers or inductors are morphogenetic hormones—steroidal hormones. These morphogenetic hormones are the chemical factors causing cellular proliferation or differentiation. They are detoxified as their corresponding glucuronides through conjugation to glucuronic acid as a result of the action of beta-glucuronidase.

51. Q. I thought that the cancer or trophoblast cell produced the beta-glucuronidase.

A. We do not believe that it does. The cancer or trophoblast cell produces neither beta-glucuronidase nor rhodanese. These are produced by the contiguous somatic cells—elicited from them in response to the presence of the syncytially produced estrogen.

52. Q. You said that rhodanese is elicited from the contiguous

somatic cells. Why doesn't this elicitation of rhodanese cancel out the cytotoxicity of nascent cyanide in the laetrile therapy of cancer?

A. We have pointed out that the cancer cells contain neither rhodanese nor beta-glucuronidase; therefore, they are susceptible to the lethal action of released HCN.

53. Q. But since both beta-glucuronidase and rhodanese are produced exterior to the trophoblast or cancer cell and by contiguous somatic cells, what is to prevent the rhodanese in the latter from detoxifying the nascent HCN to thiocyanate before it can act upon the trophoblast or malignant cell?

A. It happens that the cellular or cytotrophoblast (of which the syncytial trophoblast is an adaptation) produces the hormone gonadotrophin. As a number of workers—outside the context of Beardianism have demonstrated—chorionic gonadotrophin is an extremely powerful and specific inhibitor of rhodanese. Is this another accidental phenomenon?

54. Q. Has the action of androgen-like hormones shown demonstrable anti-carcinogenic action in man?

A. There is provocative evidence of this in the extensive use of oral contraceptives in Puerto Rico. When these studies were commenced, several Beardians predicted that the prolonged use of endocrine inhibitors to ovulation would also result in a decrease in the incidence of cancer in the women receiving these agents. Such an apparent decrease in cancer in those using these agents has occurred that the American Cancer Society has authorized the support of a full investigation of the significance of this phenomenon.

55. Q. In your explanation of the early development of the conceptus you pointed out that by the four cell stage there are three trophoblast cells, one diploid totipotent cell, and as yet no definitive embryo. The definitive embryo, you explained, finally arose as the result of the differentiation of one of a number of the diploid totipotent cells and then the remaining

diploid totipotent cells migrated into the definitive embryo, with about 80 per cent of them reaching the future gonads where, in response to estrogenic stimuli, they underwent meiosis to produce haploid gametogenous cells that upon division obligatively produced trophoblast of a genetic composition foreign to the host.

A. That is all correct.

56. Q. In view of all this, why don't we find such diploid totipotent cells in ordinary cancer if it arises through the same mechanism—in spatial or positional and/or temporal anomaly?

A. We have explained how in testicular cancer the process may proceed to the point at which a diploid totipotent cell differentiates embryo-wise to produce contiguous embryonal tissue comprising a true teratoma.

57. Q. But what happens in an ordinary cancer?

A. Since 1904 when Farmer, Walker and Moore described what they called gametoid mitosis (or meiosis) at the periphery of tumors, various workers have been describing evidence of meiosis in inflammatory and malignant tissue.

58. Q. Do you say that cancer arises as a result of simple differentiation?

A. Of differentiation, definitely: differentiation of a diploid totipotent cell through meiosis and then the differentiation of the resultant gametogenous cell obligative to division.

59. Q. I find it very difficult to accept the idea that cancers differing as widely in histology as primary uterine chorionepitheliomas, testicular chorionepitheliomas, adenocarcinomas, lymphosarcomas, leukemias, and chloromas all have an identical or constant malignant component arising all from an identical cell, by identical morphogenetic mechanisms, and differing,

perhaps, only in the initial provocative stimulus—which is still one, you claim, that is typified by estrogen. Certainly, it can not be denied that viruses produce a wide variety of animal tumors. Do you claim that an adenocarcinoma produced by a virus is identical in its constant malignant component with a leukemia also produced by a virus?

A. Before Robert Koch discovered the constant microbiological component in a wide diversity of pathological and histological states—the tubercle bacillus—medical scientists looked upon phthisis, scrofula, lupus and white swelling as utterly unrelated diseases. Now even the terminology used prior to Koch is lost. We speak simply of pulmonary tuberculosis, tuberculosis involving the lymph glands, tuberculosis of the skin, and the like. In this, not for a moment are we reasoning by analogy—which is dangerous—but rather offering an example and historical perspective. In time cancer will be known simply as the response of somatic cells to trophoblast.

As we have explained before, viruses under extraordinary conditions may act indirectly as malignant inductors. The cardinal fact in this is that their action is often highly non-specific. Hayhoe (l.c. p. 60) points out that cell-free filtrates from AKR leukemia tissue induced salivary gland tumors, while similar material from a C3H subline leukemia produced parotid tumors in some animals and subcutaneous or suprarenal tumors in others. The parotid tumors were adenocarcinomatous in type, but later tended to sarcomatous histological appearance. Extracts from induced leukemias inoculated into newborn C3H mice induced the development of leukemia in some, parotid tumors in others, and subcutaneous sarcomas in others.

60. Q. But a leukemic exhibition can not change to an adenocarcinomatous one, nor a sarcomatous exhibition to a leukemic one. No?

A. Yes; such so-called changes have been reported in both man and animals. To describe in detail the manifold instances of chorionepitheliomas grading into adenocarcinomas, or metastasizing as such, or vice versa; or to describe carcinomas grading into sarcomas, or sarcomas into carcinomas; or carcinomas and/or sarcomas yielding leukemic exhibitions; or

chloromas showing a leukemic exhibition—such a discussion in adequate detail would require an hour, half of which could be devoted to citing references.

61. Q. Is there a carcinogenic danger in the medical use of estrogen parenterally or orally administered?

A. Parenteral administration is not constant but occasional. The rest periods resulting from this procedure allow time for the "rebound of the anterior pituitary"—in its production of luteinizing gonadotrophin. Rather than being pro-carcinogenic such administration is anti-carcinogenic. On the other hand, the daily oral administration of estrogen or the implantation of subcutaneous estrogen pellets is another matter and definitely carries carcinogenic dangers because of the continuing or dysrhythmic supply of estrogen that results. On these grounds, we would give parenteral administration of estrogen—where indicated—a clean bill of health.

62. Q. Would you say, then, that the so-called malignant differentiation or induction is preceded by the induction of benign tumefaction, benign tissue?

A. Yes; this fact is a commonplace to most pathologists, surgeons, and experimental oncologists. In the experimental induction of cancer with estrogen or other carcinogens the malignant induction is preceded by papillomata on epithelial surfaces and by adenomatous hyperplasia in glands. *These are the true pre-cancerous states.* The benign tumefaction, for example, of benign papillomatosis in the lower intestinal tract in man is almost certain to be followed by malignant induction if the papillomata are not surgically removed. The subject of pre-cancerous lesions is a vast one, but in the light of the unitarian or trophoblastic thesis of cancer it is an orderly and completely understood phenomenon.

63. Q. Are there chemical agents that can handle these pre-cancerous tumefactions?

A. These should be removed mechanically or surgically.

Chemical agents may then be employed in some cases to avert the further differentiation of these truly pre-cancerous tissues.

64. Q. In the light of the unitarian or trophoblastic thesis of cancer what role does physical trauma—such as a blow to the breast or testes—play?

A. Our surmise would be that physical trauma in terms of mechanical blows is very rarely a determining factor in human cancer. If the organ is so competent in terms of susceptible tissue and organizer stimulus to undergo carcinogenesis as a result of a single blow, it is almost certain that the carcinogenic change would have occurred without the blow—though the blow might determine the site of localization. Of course, it is still possible in the light of existing experimental data to have a situation in which the physical blow could be determinative—but in practical terms this is extremely improbable. Of all tissues susceptible to malignant induction as the result of a single mechanical trauma, the testes would head the list because of their concentration of estrogen. The ovaries are, of course, protected positionally from such trauma.

65. Q. Aren't there already a number of valid cancer tests based on the detection of chorionic gonadotrophin?

A. Yes; there are. These are used routinely in almost all hospitals in the world to diagnose or follow the prognosis of uterine chorionepitheliomas and testicular chorionepitheliomas and most other testicular tumors.

66. Q. To return to the question of the practical prophylactic means that may be taken from an epidemiological, nutritional, and personal point of view, specifically what would you suggest in the light of the unitarian or trophoblastic thesis of cancer?

A. May I emphasize that in our attempt to simplify this reply it be considered always within the full context of the Beardian principles we have briefly considered. The prophylactic

measures, of all natures, are listed as follows in what I believe are of the order of their importance:

1. Exclude from the environment sources of the proved carcinogens—cigarette tars; crude coal tars and many of its derivatives; automobile exhaust wastes and the general industrial pollution of the atmosphere; protect the organism from *all* sources of radiation—fall-out, radio-active substances, ill-advised medical and dental X-rays, X-rays for shoe fitting, for mass screening for tuberculosis, etc.
2. Prevent, remove or correct as early as possible any pre-cancerous lesions (benign hyperplasia and hypertrophy of somatic cells). These include papillomata and polyps of all types, adenomas of glandular tissues; any abnormal alterations in gross structure of skin or mucous membranes; endometriosis; cystic ovaries; mastitis; hyperestrogenism in general—a somewhat vague term; hyperplastic changes in the thyroid gland; abnormalities in the menstrual cycle; cryptorchidism; etc. In other words, vigilant attention to *any* abnormal hyperplasia, hypertrophy, or anatomical abnormality, however slight.
3. The maintenance of normal hepatic function for the facilitation of estrogen detoxification and the detoxification of related steroids. Such normal function is maintained by avoiding toxins that induce cirrhosis and the associated depression in liver function. These toxins are alcohol (in the absence of adequate B vitamins), heavy metals, carbon tetrachloride, a wide range of industrial solvents. Since infectious hepatitis decreases hepatic detoxification of estrogen, this problem should be prosecuted more energetically by public health people. In certain parts of the world parasitization of hepatic tissue produces demonstrable hyperestrogenism.
4. Nutrition is an important factor, though this subject has unfortunate connotations due to cultism. Deficiencies in the vitamin B complex cause hyperestrogenism in both experimental animals and man. Care should be taken to obtain the maximum intake of all the B vitamins consistent with optimum nutrition. Emphasis should, of course, be placed on high grade proteins in the diet. Extensive statistical data prove that a reasonable limitation in caloric intake is

anti-carcinogenic. Excessive caloric intake, as associated with obesity, is pro-carcinogenic. Starvation regimens, on the other hand, are pro-carcinogenic over prolonged periods of time if they involve deficiencies in proteins and B vitamins.

5. Scrupulous avoidance of *all chronic inflammations* is important. This refers not only to the surface membranes but to the gall bladder, appendix, oropharynx, uterus, prostate, gastro-intestinal tract, and other parts of the body. Surgical science can do much to remove such possibly pre-neoplastic conditions.
6. The utilization of modern cytological technics—smear test—before signs or symptoms have developed as a part of the periodic health examination.
7. The periodic testing of the body fluids for chorionic gonadotrophin by some of the new pioneer technics (which have not yet come into general acceptance): trypsin inhibitor tests, chymotrypsin inhibitor tests, Roffo Test, Beard Anthrone Test, and the modifications of the latter. Determinations on rennen inhibitor might also be advisable. It is to be hoped that the direct test for the immunological identification of chorionic gonadotrophin will become clinically practicable during the coming year. This area is still in the pioneering stage.
8. The development of physicians trained in the unitarian or trophoblastic thesis of cancer—or equivalently trained in the biology, biochemistry, endocrinology, comparative embryology, and genetics of cancer. Such men will be in a position to reach medically independent conclusions on the advisability, on the basis of certain assays, of using prophylactically oral preparations of physiologically balanced crystalline pancreatic enzyme preparations as substitution therapy in those with exocrine pancreatic deficiency.
9. The incorporation in the diet of fruits and vegetables rich in natural laetries (beta cyanogenetic glucosides and glucuronosides). The nutritional utilization of apple seeds, seeds of various fruits of the *Prunus* family, certain grasses etc. While the geography of cancer is a notoriously inexact science at present, there are data highly suggestive of the thesis that in tropical areas where over one-third of a

vegetable materials contain rich concentrations of natural laetriles the incidence of cancer is lower than in areas not so favored.

67. Q. If you showed a highly positive chorionic gonadotrophin reaction according to Beard Anthrone Test, what would you do?

A. I would have additional urine specimens submitted under other names. If these were consistently positive, I would seek a thorough physical examination. If this disclosed nothing, I would have chymotrypsin and trypsin inhibitor tests run. If these were suspicious or positive, I would have the original Roffo test repeated.

68. Q. Suppose no lesions were found on physical examination but that all of these other tests remained highly positive?

A. I would go to my physician for intravenous injections of Laetrile, 1,000 mg., at twice weekly intervals and take orally adequate crystalline pancreatic enzyme preparations. At the end of a five week period I would rest from all prophylaxis for ten days and then resubmit urine and other specimens.

69. Q. Suppose on physical examination a lesion were found—an early cancer of the lung or stomach—what would you do?

A. After a very careful diagnostic work-up by highly competent people, I would then ask that Laetrile, 1,000 mg., be administered intravenously at thrice weekly intervals. I would also take oral doses of pancreatic enzymes as prescribed by my physician. As a Beardian, I would be especially intense in following my objectively reported clinical status on a week-to-week basis. Under the hypothetical situation we are discussing, I would rely strongly upon the tests I have described because if they had proved capable of leading to a diagnosis of a condition that might have been missed, I could reasonably expect a diagnostic consistency in them that would tell my doctor of any amelioration or exacerbation that occurred.

70. Q. Will the influence of Beardianism extend beyond the sciences?

A. It will in a way similar to the influence of Darwin, Freud or Marx. Beard, for example, was one of the first to show the autonomy of the germ cells from the body cells and scientifically to substantiate the thesis that the individual is but a temporary harbor for an almost immortal procession of germ cells that link one generation with the next. Beard also showed us that there are apparently no intrinsically malignant or evil or diseased cells or processes in the natural order of things. All such appearances represent a positional and/or temporal anomaly of basically normal living units—a matter of their being at the wrong place at the wrong time. Indeed, the cell that in spatial and temporal anomaly we have often described as the epitome of disorder, disease, and caprice, represents a cell so exquisitely normal that without it in its normal canalization human life itself could not exist. This cell is now amenable to thoroughly understood natural laws, and its pathological exhibition is destined to become an historical curiosity.

71. Q. It seems that you avoid the discussion of viruses as etiologic agents in human cancer? What is the relation of the unitarian or trophoblastic thesis of cancer to this question?

A. As we have previously pointed out, the unitarian or trophoblastic thesis of cancer is the only explanation so far advanced that has ever been able to show how under extraordinary circumstances viruses could participate in carcinogenesis in man. The virus of infectious hepatitis, for example, is known to cause hepatic damage. Significant increases of biologically active estrogen have been found in men with acute infective hepatitis (Edmondson, Glass and Soll, 1939; Glass, Edmondson and Soll, 1940-3).

Such excessive and persisting quantities of estrogen, of course, are potentially carcinogenic in the human male.

This is as close as anyone has come to any evidence of the direct or indirect participation of viruses in human carcinogenesis. No one has ever been able to isolate a single virus from a human cancer; to demonstrate any evidence of the infectivity of any human cancer; nor produce any substan-

tially suggestive evidence that a virus could directly participate in human carcinogenesis. This is despite the fact that outside the context of the unitarian or trophoblastic thesis of cancer the presumption is that cancer comprises a multiplicity of diseases each with its own etiological agent, presumably a virus. Despite the postulated multiplicity of carcinogenic viruses in man, there is no evidence whatever for such a notion. The idea is, indeed, one of the most lugubrious delusions in biology and plain logic.

In the "Conference Discussion" on a paper by the late Francisco Duran-Reynals and Edward Shrigley on "Virus Infection as an Etiologic Agent of Cancer" (A.A.A.S. Research Conference on Cancer, F. R. Moulton, Ed., Am. Assn. Advancement of Sci., Washington, 1945), M. B. Shimkin observed: "I am afraid that the concept of the virus etiology of tumors is sometimes more of a religion than a science."

W. R. Earle of the National Cancer Institute added, "These points, among others, suggest to my mind that cell changes associated with the action of methylcholanthrene are quite possibly of the same category as those seen in cell differentiation of the organism. Tentatively, at least, I am inclined to conceive of such carcinogenic changes as a type of aberrant differentiation." Of this, any Beardian would ask (1) aberrant differentiation from a cell in the life cycle? or (2) to a cell with a normal counterpart in the life cycle? or (3) to the most primitive cell in the life cycle and from the most undifferentiated cell in the life cycle? If not such cells, from what cells?



QUESTIONS & ANSWERS ON WORK DONE BY DR. D.R.S. KIRBY, OXFORD UNIVERSITY, ON TROPHOBLASTIC TRANSPLANTS AS PUBLISHED IN NATURE

A Response by Ernst T. Krebs, Jr.

June 8, 1962

Q. Have you reprints of the paper from NATURE?

A. These have not yet arrived. We expect them shortly. Our comments are based on a popular report by Delos Smith, U.P. International. Since we are intimately acquainted with the work, we can allow for obvious limitations in the press report.

Q. The report by Delos Smith says that trophoblast "Cells Eat Cancer." If cancer is trophoblast, how can implanted trophoblast cells eat a malignant mammary tumor in a mouse?

A. We have frequently emphasized the low level of malignancy in non-metastatic mammary tumors in mice; at last 90 per cent of the bulk of such tumors comprises non-malignant somatic elements of an embryonal nature. Less than 10 per cent of such a tumor comprises definitively malignant or trophoblast cells.

Q. Aren't trophoblast cells embryonal?

A. No; they are the very antithesis of embryonal cells and will destroy embryonal cells.

Q. Why was the pregnancy trophoblast implanted into malignant mammary tumors?

- A. One could expect implanted trophoblast to grow in such tumors because the hostal tissue has already been prepared by the endogenous trophoblast of the tumor and thus provides a congenial decidua for the added trophoblast. The added trophoblast that destroys or "eats" the mammary tumor destroys or "eats" the definitively benign or somatic elements in such a tumor, not the malignant elements.
- Q. Why does Kirby describe the power of trophoblast "to destroy the maternal tissue" as self-limited?
- A. His statement is true but semantically dangerous. He should emphasize very carefully that the so-called "self-limitation" is extrinsically imposed by hostal tissue and is NOT intrinsic to the trophoblast. The classical observations of Maximov dramatically portray this fact.
- Q. "Will trophoblast from one mammalian species destroy mammary cancer cells in another mammalian species?" Kirby asks.
- A. Human trophoblast from primary uterine chorionepithelioma has already been successfully transplanted to the buccal pouch of hamsters. The lower we go in ontogeny the less immunological barrier we find between species. Trophoblast is the first or earliest tissue in the ontogeny of the definitive mammalian conceptus. It appears, of course, before the first vestiges of the definitive embryo. Since the definitively malignant cells in ANY malignant growth are trophoblast, it is unlikely that trophoblast of one species will destroy the trophoblast or the definitively malignant cells of another species, but such hererologous trophoblast will destroy the somatic component of the hostal tumor and thereby so disrupt the architectonics of the tumor as to induce a necrosis that will involve definitively malignant or trophoblast cells (with the overwhelming bulk of hostal embryonal or benign cells comprising the tumefaction.)
- Q. What is the significance of J. B. Murphy's observation that placental extracts caused regression of mammary tumors in 26.7 per cent of treated mice and complete disappearance in 21.3 per cent?

- A. Of all tissues of the body, the somatic elements of the placenta are of necessity the richest in the elements that check trophoblast growth. Since the definitively malignant cells in cancerous lesions are trophoblast, it follows that their growth will sometimes be checked or that they may even be destroyed following the injection of placental extracts containing these factors.
- Q. Who is the scientist that Kirby says in 1902 compared cancer cells to trophoblast cells?
- A. John Beard in *Lancet*, i:1758-1761 (1902) in a paper entitled "The Embryological Aspects and Etiology of Carcinoma" first concluded, on extensive experimental grounds, that cancer is trophoblastic. The mammalian trophoblast having been first described in 1887 by Hubrecht in the hedge hog was still almost completely unknown. Roger Williams, an English physician, around 1904, also independently concluded that cancer is trophoblast, though his conclusions were based on an inadequate knowledge of morphogenesis.
- Q. If normal pregnancy trophoblast transplanted into a mammary tumor destroys such a tumor, are we not justified in concluding that such trophoblast is even more malignant than the tumor?
- A. This question is asked in the erroneous or non-Beardian context. The constant malignant component in all exhibitions of cancer is trophoblast. The malignancy of a tumor is directly proportional to its concentration of trophoblast; therefore, if fresh trophoblast is added to a tumor that already may comprise only 5 to 10 per cent actual trophoblast, the added trophoblast will proceed to increase the rate at which somatic or non-malignant elements comprising 90 per cent of the tumor is destroyed by trophoblast. We want also to remember that while trophoblast is antithetic to the hostal soma, the soma is also antithetic to the trophoblast. The somatic antithesis is expressed in tumefaction, which is actually a hostal protective reaction. This is why those malignant lesions with the least tumefaction are usually the most malignant while those with the most tumefaction are usually nearest to benignancy. The

trophoblastic or unitarian thesis does not hold that normal pregnancy trophoblast is more malignant than any known malignant tumor. It does recognize that the most malignant exhibitions *in vitro* and *in vivo* comprise pure or frank trophoblast simply because the higher the concentration of trophoblast present the higher the malignancy of the exhibition; and the less trophoblast present the lower the malignancy of the exhibition. Add trophoblast to an existing malignant lesion and such trophoblast will increase the malignancy of the lesion to the point of destroying the reactive or defensive benign somatic tissue by which the host resisted in part the original trophoblast.

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The foregoing references, without exception and including those from the world's most prestigious journal in the field of oncology, are positive reports on the safety and effectiveness of Laetrile (nitriloside), and describe completely non-toxic palliation and other beneficial effects of Laetrile (nitriloside) in abolishing pain and fetor where present, decreasing and eliminating the need for narcotics, and extending life-expectancy of cancer patients left terminal by surgery and/or radiation.

For the completeness of this bibliography, we also cite the single negative report on Laetrile, published ten years ago and obviously designed to disparage continued study or investigational use of Laetrile. The said single negative report on Laetrile, which is based upon the observations of unidentified investigators in unidentified institutions administering a purported "Laetrile" not obtained from the only source of the material, is to be found in *California Medicine*, 78:320 (1953).

E.T.K., Jr.

GLOSSARY

adenopathy—a swelling of glands

Beardian—pertaining to the work of John Beard (1858-1924), Scottish embryologist at the University of Edinburgh, who discovered that the cancer cell is the trophoblast cell

benign—not endangering health or life, as opposed to malignant

beta-glucosidase—an enzyme which acts upon glucosides, causing them to break down

biochemistry—the branch of chemistry relating to the life processes, their mode of action and their products

biopsy—the removal and examination (usually microscopic) of a piece of tissue from the living body, especially for diagnosis

cancer cell—(see trophoblast cell)

carcinogen—a substance or agent initiating development of the malignant process

carcinoma—a cancer growth

chymotrypsin—a pancreatic enzyme of the trypsin group; it acts upon trophoblast cells to destroy them

diploid totipotent cell—a cell with the full complement of chromosomes (46 in humans) and with the ability to produce a whole being

embryology—the science which deals with the origin, structure and development of the embryo

endocrinology—the branch of medicine relating to endocrine glands, which influence physiological activities

enzyme—a complex organic substance produced by cells and having the power to initiate or accelerate specific body chemical reactions

estrogens—in general, the sex hormones

haploid gametogenous cell—a cell possessing half (23) of the normal chromosomes; it arises upon the meiotic division of a diploid totipotent cell

hormones—complex chemical compounds evolved in one part of an organism and carried by the blood system or body fluids to other parts where they exercise specific physiological actions

life cycle—pertaining to the processes and organism involved in the continuation of life

malignant—threatening to life; cancerous

meiosis—the process of cell division in which the number of chromosomes is reduced from diploid (46) to haploid (23)

mitosis—the process of cell division in which the full complement (46) of chromosomes is retained

metastasis—the transfer of disease from one part of the body to another, with development of the characteristic lesion in the new location, as in cancer

necrosis—the death of a part of the body

palliative—providing relief

pancreas—a gland connecting with the alimentary canal; it produces enzymes and hormones

pharmacology—the science of the action of medicines

rhodanese—an enzyme with the ability to deactivate cyanide

slough—dead tissue separated and thrown off from the living parts of organs

soma—all of any organism except the germ cells

spontaneous regression—applied to tumors which recede for unknown reasons

terminal case—in cancer, a patient in the final stages of the disease

toxicity—having poisonous effects

transplantation—the implanting of tissue from one body to another

trophoblast cell—the most primitive cell in the life cycle, arising on the second meiotic division of a diploid totipotent cell; in

pregnancy, the trophoblast is the early means of providing nourishment to the embryo; outside of pregnancy, the trophoblast exhibits itself as cancer.

Unitarian Thesis—in cancer, pertaining to the Beardian principle that the trophoblast cell and the cancer cell are one and the same

zygote—the product of the fertilization of an ovum by a spermatozoon

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