IN THE MATTER OF

A RULEMAKING PROCEEDING

CONCERNING LAETRILE

City of Rockville )
State of Maryland  )

Docket No. 77N-0048

AFFIDAVIT OF THOMAS H. JUKES, Ph.D.

Before me personally appeared Thomas H. Jukes, Ph.D., D.Sc., who being first duly sworn, deposes and says:

1. I am Professor-in-Residence, Medical Physics and Research Biochemist, Space Sciences Laboratory, University of California, Berkeley, California.

2. I received a Doctor of Philosophy Degree in Biochemistry from the University of Toronto in 1933.

3. I was a National Research Council Fellow in Medical Sciences, University of California, Berkeley, 1933-1934; Instructor and Assistant Professor, University of California, College of Agriculture, Davis, 1934-1942; Director of Nutrition and Physiology Research and Director of Biochemistry, Lederle Laboratories, American Cyanamid Company, 1942-1963; and Visiting Senior Research Fellow in Biochemistry, Princeton University, 1962-1963.

4. I am a member of the American Society of Biological Chemists, American Institute of Nutrition (Council, 1941-1946; Fellow, 1973), American Chemical Society, American Society of Animal Science, Society for Experimental Biology and Medicine (Editorial Board, 1953-1958), and Biophysical Society.

6. My fields of research include the following: Vitamin B complex (especially riboflavin, nicotinic acid, pantothenic acid, vitamin B-6, choline, folic acid, and vitamin B-12), folic acid antagonists in cancer chemotherapy, antibiotics in nutrition, nutritional deficiencies, amino acid code, protein chemistry, molecular evolution, and non-Darwinian evolution.

7. I am the author of the books B-Vitamins for Blood Formation, Antibiotics in Nutrition, and Molecules and Evolution, and more than 250 articles in scientific journals.


9. My curriculum vitae is attached hereto as Exhibit 1. It provides a summary of my education, training, and experience.

10. I wrote an article entitled "Laetrile for Cancer" which was published in the Journal of the American Medical Association on September 13, 1976. In this article, I discussed the subject of cancer quackery, particularly as it applies to amygdalin or laetrile. A copy of my article is attached as Exhibit 2.

11. As part of my research, I am familiar with the nutritional biochemistry of the B-vitamins and the biochemistry of the cyanogenic glycosides. In my article entitled "Laetrile for Cancer" (Exhibit 2), I discussed the biochemistry of these glycosides and stated that the cyanogenetic glycosides have no food value or vitamin activity, although the misnomer vitamin B-17 is used in the promotion of laetrile.

12. I have read the deposition and attachments thereto of Dean Burk, President of the Dean Burk Foundation, Inc., dated March 25, 1977,
submitted as part of the Food and Drug Administration's Administrative Rule Making Hearing on Laetrile. I have known Dean Burk personally for forty years. It is with a deep sense of regret that I have noted his recent attachment to the cause of laetrile. The fact that he is scientifically well qualified as a biochemist does not add credence to his claims for laetrile; instead, it serves to underscore the tragedy that he has betrayed his scientific training to make such preposterous statements as are contained in his deposition.

13. On page 1, paragraph 5, of his deposition, Dr. Burk states that he "performed tens of thousands of experiments with laetrile". He also says (correctly) that "he has published 300 scientific papers". None of the scientific papers by Dr. Burk that I have seen in an accredited journal dealt with laetrile. Therefore, I conclude that the majority of the time he spent on scientific research that resulted in the said papers did not deal with laetrile. This conclusion is supported by the fact that he started publishing prior to or around 1930, many years before laetrile appeared on the scene.

The term "tens of thousands" must imply a multiple of ten and consequently, a minimum of 20,000. If Dr. Burk has carried out 20,000 experiments on laetrile, and if each of these experiments occupied one day, which is a much shorter time than is usually necessary for an experiment in nutritional biochemistry or cancer research, he would have to do 300 experiments per year of 300 working days. This would need a minimum of 67 years for 20,000 experiments. It is, therefore, my conclusion that this statement is palpable falsehood.

14. On page 2, paragraph 7, Dr. Burk asserts that amygdalin is Vitamin B-17. Amygdalin is not a vitamin in even the remotest sense of the term. Amygdalin is a cyanogenetic glycoside, a toxicant occurring naturally in foods. Vitamins are nutritionally essential substances that are needed in the diet of vertebrate animals to prevent nutritional deficiency.
diseases. By definition, amino acids and minerals are excluded from the term "vitamins". The key to the term "vitamins" is that the absence of vitamins from the diet in an experimental animal or a human being must lead to the appearance of a nutritional deficiency disease, which is prevented or cured by adding the vitamin to the diet. Laetrile has no such property.

15. I would describe the properties of vitamins as follows:

A. The name "vitamin" was coined by Dr. Casimir Funk in 1912. He had the idea that certain diseases, such as scurvy, pellagra and beri-beri were caused by inadequate diet and not by microorganisms or parasites. He concluded that there was a specific substance in food that would prevent or cure each of these diseases. So he said that for scurvy there is an antiscurvy vitamin, for pellagra there is an anti-pellagra vitamin, and so on. Funk's idea was essentially correct.

However, there are some nutritional deficiency diseases, such as anemia due to iron deficiency and goiter caused by a lack of iodine, that are caused by a lack of minerals. These are quite similar to vitamin deficiency diseases, but minerals are not classed as vitamins. Vitamins are carbon compounds, and all compounds with carbon are called "organic chemicals". Therefore, vitamins are organic chemicals. Nearly all vitamins are manufactured by green growing plants. The exceptions are Vitamin D and Vitamin B-12. Another property of vitamins is that they are needed in the diet in only small amounts, a few milligrams a day or even less. One milligram is about one thirty-thousandth of an ounce.

B. Vitamins are defined as being needed by vertebrate animals. This distinguishes them from other, similar substances that are needed only for the growth of microscopic organisms called protozoa that belong to the animal kingdom. Deficiencies of vitamins can be produced experimentally
in animals or, sometimes, in volunteer human subjects by feeding purified deficient diets. When the deficiencies appear, they can be promptly cured by feeding or injecting the missing vitamin.

C. Vitamins are present in the tissues of animals, such as the muscles, blood and liver, and vitamins enter into biochemical reactions in the body. In vitamin deficiencies, the amount present in the body becomes reduced, and this may be shown often by analyzing the blood.

D. To establish a vitamin as actually existing, several steps are necessary. The first step is publication in a recognized scientific journal of experimental work, including a complete and repeatable description of the procedures used in the research. This is followed by confirmation by other scientists, or lack of confirmation. The other scientists also publish their findings in scientific journals. Such journals require that manuscripts be reviewed by other scientists before publication. The burden of proof in establishing the existence of a vitamin is up to the scientists who claim that it exists. Sometimes the work cannot be repeated, even after a number of tries. In such cases, the existence of the vitamin is not recognized, and claims for it are not accepted. This has occurred in the case of some of the B vitamins, including the so-called vitamins B-13 and B-14.

E. If the vitamin has crossed the preceding hurdles, there will be an extension of the research, including analysis of foods for its presence, isolation of the vitamin in pure form, determination of its exact chemical molecular structure, and demonstration of the effectiveness of the pure, usually crystalline, preparation of the vitamin. Finally, chemical synthesis of the vitamin is carried out by organic chemists, and the results are not accepted until it is shown by exhaustive chemical and biological tests that the synthetic and natural vitamins are identical. Such synthesis and testing has been carried out for all the accepted vitamins. The last and most difficult to be synthesized was Vitamin B-12. This was also the last of the vitamins to be discovered.
F. The next step is that the Food and Nutrition Board of the National Academy of Sciences sets up Recommended Daily Allowances through its committees on this subject. These include allowances for both human beings and domestic animals. The Recommended Daily Allowances are estimated to exceed the requirements of most individuals. They are considered to be adequate to meet the known nutritional needs of practically all healthy persons.

G. The last step is adoption of the Recommended Daily Allowances by the Food and Drug Administration. The Recommended Daily Allowances for the vitamins listed by the Food and Drug Administration are as follows: These are the allowances for adults and children four or more years of age:

<table>
<thead>
<tr>
<th>VITAMIN</th>
<th>UNIT OF MEASUREMENT</th>
<th>ADULTS &amp; CHILDREN 4 OR MORE YEARS OF AGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td>International Units</td>
<td>5,000</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>International Units</td>
<td>400</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>International Units</td>
<td>30</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Milligrams</td>
<td>60</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>Milligrams</td>
<td>0.4</td>
</tr>
<tr>
<td>Thiamine</td>
<td>Milligrams</td>
<td>1.5</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>Milligrams</td>
<td>1.7</td>
</tr>
<tr>
<td>Niacin</td>
<td>Milligrams</td>
<td>20</td>
</tr>
<tr>
<td>Vitamin B-6</td>
<td>Milligrams</td>
<td>2.0</td>
</tr>
<tr>
<td>Vitamin B-12</td>
<td>Micrograms*</td>
<td>6</td>
</tr>
<tr>
<td>Biotin</td>
<td>Milligrams</td>
<td>0.3</td>
</tr>
<tr>
<td>Pantothenic Acid</td>
<td>Milligrams</td>
<td>10</td>
</tr>
</tbody>
</table>

*One microgram is one thousandth of a milligram.

In addition to these, Vitamin K and choline are also recognized by the Food and Nutrition Board but Recommended Daily Allowances have not been set. These two substances are present in many common foods.
16. In my article "Laetrile for Cancer" (Exhibit 2), I have documented the fact that the term "vitamin B-17" was introduced into the nomenclature of amygdalin as a subterfuge and a sales device, and was not based on any experimental findings. I repeat this statement for the purposes of my affidavit since there are no data available to show that a disease state is produced or alleviated by the exclusion from an addition to the diet of amygdalin.

17. In paragraph 9 of his deposition (page 3), Dr. Burk states that Amygdalin is a food in the GRAS list. This and other statements in paragraph 10 are without merit or substance. The mere inclusion of preparations obtained from bitter almond and apricot or peach kernels in the GRAS list does not even suggest that amygdalin is safe. The bitter almond preparation on the GRAS list is oil of bitter almonds, free from prussic acid (hydrocyanic acid). The oil is made free from prussic acid by hydrolyzing the amygdalin in bitter almonds, and removing the cyanide by volatilizing it. This procedure leaves benzaldehyde as a residue, and the characteristic odor of the oil is due to benzaldehyde. Laetrile is sold in tablet and injectable forms, not as an oil free from prussic acid which is to be used as flavoring for food. The plain fact is amygdalin (Laetrile) is not on the GRAS list.

18. In paragraph 11 of his deposition (page 4) Dr. Burk states that Laetrile is nontoxic over a very wide range of application. It is generally true that amygdalin does not exhibit acute toxicity in animals and man at comparatively high dosage. However, this statement is true only under certain conditions. I must expound on this point, because it is crucial. The molecule of laetrile contains cyanide, which is a deadly poison when it is set free from amygdalin by an enzyme system that is present in plants, but not to a significant or effective extent in mammals as represented by human beings, rats, and mice. The action of the enzyme system takes place in two steps. The first step is carried out by the enzyme beta-glucosidase.
This separates mandelonitrile, \( C_6H_5CHCN \), from the two molecules of glucose that are present in amygdalin. In the second step, mandelonitrile is hydrolyzed to benzaldehyde, \( C_6H_5CHO \), and hydrogen cyanide (prussic acid) HCN.

As a result of this biochemical change, the consumption of apricot milkshakes and bitter almonds produces well-documented cases of cyanide poisoning, some of which have been fatal. Reports of two such examples are attached (Exhibits 3 and 4). The consumption of amygdalin by mouth is therefore potentially unsafe. Its safety depends upon the simultaneous absence of the enzyme system. This is further documented in the publication by Laster and Schabel (Cancer Chemotherapy Reports, 59:951, 1975), in which addition of beta-glucosidase to a regimen including the oral administration of laetrile caused the appearance of toxic symptoms in rats. Laster and Schabel state, "Potentiation of the lethal toxicity of amygdalin \( MF \) by beta-glucosidase was observed in all studies where the two agents were given in simultaneous combination".

19. It is pertinent to compare laetrile with a closely similar substance, linamarin, which occurs in the widely used tropical food, cassava. The formulas of amygdalin and linamarin are found in Exhibit 5. Both of them set free hydrogen cyanide upon enzymatic treatment. The presence of linamarin in the diet of certain Africans leads to the widespread occurrence of tropical atoxic neuropathy, often resulting in blindness. This is caused by chronic cyanide poisoning resulting from the breakdown of linamarin (Exhibit 5).

20. Most items used as foods are not safe for injection, and amygdalin under the name, "laetrile", is frequently injected into cancer patients, apparently, without immediate toxic effects. The toxic effects of injecting foreign substances may not show up for months or years. To be safe for injectable purposes, a compound must be shown by means of long-term toxicity tests not to produce pathological changes. No such data are available for amygdalin.
21. In paragraph 12 of his deposition (page 4) Dr. Burk cites what he terms "a widely accepted definition of vitamins and their varying natures and background and interpretation". This citation has not been subjected to peer review and is not scientifically valid or accepted. For example, Burk says that on page 8 of his cited reference "it becomes almost impossible, on the negative side, ever to declare scientifically that a given compound is not a vitamin for some organism(s) somewhere and hence ever to declare scientifically that 'said given compound is not a vitamin' ..." (emphasis added). This statement is sophistry and balderdash. Under its terms, I could state that castor oil, or bourbon whiskey, or nicotine was a vitamin simply because Burk states that such a statement is impossible to disprove. This kind of double-talk is scientific nihilism.

It is possible to show whether a substance is a vitamin by performing necessary studies to determine the effect created by withholding the substance from the diet. When no effect is observed, it is safe to infer that the substance is not a vitamin.

22. It is particularly important to define vitamins closely in this era of health food promotion and nutritional rackets. Professor David Greenberg's definition of a vitamin, cited by Burk in paragraph 12, is as follows:

(a) It is a nutritional component of organic composition required in small amounts for the complete health and well-being of the organism.

(b) Vitamins are not utilized primarily to supply energy or as a source of structural tissue components of the body.

(c) A vitamin functions to promote a physiological process or processes vital to the continued existence of the organism.

(d) A vitamin cannot be synthesized by the cells or the organism and must be supplied de novo.

(e) In man and in other mammals, deficiency of a specific vitamin is the cause of certain rather well-defined diseases. These include scurvy, beri-beri, pellagra, pernicious anemia and rickets. These diseases are prevented or cured by addition of the appropriate vitamin.
Professor Greenberg did not make in this article "a studied neglect" of the "vitaminic nature of laetrile". No such vitaminic nature of laetrile has been shown to exist.

23. In paragraph 13 of his deposition (page 4), Dr. Burk refers to his brief in support of laetrile (Burk's Exhibit A) which, is a self-serving, rambling discourse. "Exhibit A" has not been published in a reputable scientific journal. Dr. Burk well knows the rules of scientific publication; he has followed them in the past, and apparently, he has now abandoned them in his strenuous efforts to promote laetrile. Exhibit A is nothing more than a collection of assertions, theories, and quotations arranged in argument form to make the best possible case for laetrile. This paper is devoid of scientific data to demonstrate that laetrile is a vitamin; that there are "deficiency lesions" attributable to the absence of laetrile from the diet; and that laetrile has efficacy against cancer. Indeed, Dr. Burk at page 15 of Exhibit A selectively cites research at Sloan Kettering Cancer Center and Southern Research Institute to support the efficacy of laetrile when such data fail to suggest that laetrile possesses any antineoplastic activity. Other Burk references to research on laetrile do not include citation to the medical or scientific literature, which would enable the reader to assess the research Dr. Burk relies upon, or cites to obscure journals which contain anecdotal reports of uncontrolled use of a substance which may contain amygdalin: e.g., Exhibit A, page 11, reports on the use of amygdalin in the years 1845-1846.

24. Burk's Exhibit F is unacceptable as evidence. Indeed, it is not amenable to evaluation. It consists of a single xeroxed page without statements of authorship, without autopsy details, and without pathological description. If Dr. Burk's thesis is that cancer is a deficiency lesion caused by the absence of laetrile from the diet, Exhibit F fails to support
that thesis, for Exhibit F does not even say what diets the animals received. Furthermore, in Exhibit F it is stated that the animals were injected with a "1:6 Walker 256 carcinoma homogenate". This is a transmissible tumor, and, therefore, if the animals developed cancer, they cannot be said to have developed it as a result of a nutritional deficiency in the diet. For the same reason, Burk's exhibits setting forth work at Sloan-Kettering (Exhibit D) and Southern Research Institute (Exhibit E) fail to support the thesis that cancer is caused by a laetrile deficiency. Work at those institutions was not designed to demonstrate a deficiency state and, in fact, the researchers there did not purport to draw such inferences from their data. Nor do the data support such inferences since the test animals were not shown to be on a pure laetrile-free diet.

25. In Burk's deposition, paragraph 14 (page 4), the statement that "clear-cut published data indicating a positive and vitamin action" was reported and republished by a California State Department of Health Advisory Board in 1963 is untrue. To the contrary, the report indicated that laetrile was ineffective, but exerted an effect as a placebo. In this regard statements such as "in a study of 44 terminal cancer patients ... all of the physicians whose patients were reviewed spoke of increase in the sense of well being and appetite" are not evidence of drug efficacy or vitamin effect. Such statements merely summarize anecdotal experience.

First, the placebo effect in cancer is well known: patients who receive inert medication often "feel better". Second, cancer must be accurately diagnosed before data on its so-called "alleviation" are acceptable. Third, the clinical trials must be controlled. Many case reports of patients receiving laetrile have subsequently been found to include other forms of therapy. Until elementary criteria such as these are satisfied, the anecdotes are irrelevant.

26. Phrases in Burk's deposition (page 5) such as "in forthcoming weeks a book will appear" and "results of which must be awaited" do not contribute to the resolution of this question. Such statements are the salesman's talk in trade, not the scientist's.
27. I will now proceed to comment on the voluminous list of exhibits appended to the deposition by Burk:

A. Exhibit A: (The first of these is Exhibit A, "Vitamin B-17, Vitamin B-15, Vitamin B-13, A Brief on Foods and Vitamins", McNaughton Foundation, June 1975).

1. Page 3 of Pamphlet (Summary), General Comments

Burk defines amygdalin as synonymous with nitriloside, laetrile and Vitamin B-17. He is wrong in stating that it is a food. Amygdalin belongs to the class of compounds termed "toxicants occurring naturally in foods". Amygdalin is so defined and described in the book TOXICANTS OCCURRING NATURALLY IN FOODS, published by the National Academy of Sciences, Washington, D.C., 1973. Amygdalin in its pure state is of comparatively low toxicity, but it contains cyanide that is readily liberated by hydrolysis. This often results in poisoning caused by sources of amygdalin, such as bitter almonds or apricot seeds. There are many other cyanogenic glycosides in addition to amygdalin. These include, as an example, linamarin, present in cassava, and often responsible for poisoning the consumers thereof. Other toxicants naturally in foods are arsenic, lead, cadmium, mercury, oxalates, hallucinogens that are present in nutmeg and certain mushrooms, alkaloids, such as solanine in potatoes, that are toxic in moderate overdosage, and many others. Webster's dictionary definition of food is as follows: "material consisting of carbohydrates, fats, protein and supplementary substances (as minerals, vitamins) that is taken or absorbed into the body of an organism in order to sustain growth, repair, and all vital processes and to furnish energy for all activity of the organism". This definition is quite satisfactory, and it does not include toxicants such as amygdalin.

Drugs are substances other than foods, intended to diagnose, prevent, treat or cure disease or to affect the structure or function of the body of man or other animals. However, drugs may be substances that can be extracted from foods, purified, and used for drug purposes.
The statutory definition of "food" used by Burk at the foot of page 3 is unsatisfactory for understanding because it says that the term "food" means articles used for food. While this is a circular definition when carried to extremes -- no one argues that crushed glass is a food although some circus people eat glass -- the definition is still satisfactory since amygdalin is not used as food. Those who eat foods for the purpose of ingesting amygdalin do so not for food purposes, but rather to prevent or cure cancer, which is, of course, a drug use.

2. On page 8, Burk's definition of a food shows that he evidently does not understand the relationship between sulfonamides, para-aminobenzoic acid, and folic acid. This is as follows. Human beings need folic acid as a vitamin. In contrast, certain bacteria manufacture folic acid from para-aminobenzoic acid. The growth of these bacteria is inhibited by sulfonamides, which block the synthesis of folic acid from para-aminobenzoic acid. This is why sulfonamides are useful drugs against bacterial diseases. However, sulfonamides have no effect on the synthesis of folic acid by human beings and other vertebrate animals, because such animals do not synthesize folic acid but instead they must obtain it from their food. So folic acid is a vitamin, and para-aminobenzoic acid is not a vitamin.

3. On the top of page 8, the definition of vitamins given here by Burk is incorrect, in that he states that they are required by "any given living organism (animal, plant or microorganism)." Vitamins are substances needed by vertebrate animals. Growth factors required for invertebrate animals such as protozoa, by plants, and by microorganisms do not come within the definition of vitamins. Examples of such "non-vitamins" are lipoic acid (thioctic acid), biopterin, and para-aminobenzoic acid. These are not vitamins. They are growth factors for microorganisms.

4. The second paragraph on page 8 is also erroneous. Consensus is obtained on the nomenclature of vitamins. The last vitamin to be discovered and named was Vitamin D-12 in 1948. It is true that, as Burk says, a consensus can be upset by a new discovery. However, this generalization
does not support the validation of claims that are patently erroneous. In this regard, we often hear arguments similar to that of Burk. For example, a Dr. Benjamin Frank, who has written a book saying that eating DNA will reverse the aging process, compares himself with the Wright Brothers, who constructed and flew an airplane when experts said it was scientifically impossible. The response to this is that it is easier to make a claim than to invent the airplane. The graveyards of science contain many unsubstantiable claims for vitamins that have been buried. Burk’s support of Vitamin B-17 does not make him comparable with Newton and Pasteur because these great men made new discoveries that conflicted with the current opinion. See page 9, Exhibit A. Once again, there are many would-be innovators, but only one Newton.

5. On the bottom of page 9, Burk uses the name Vitamin B-17 to apply generally to cyanophoric glycosides (cyanogenic glucosides). On page 10 he makes the astounding statement that Vitamin B-17 is a notable constituent of the "diets of wild carnivores and herbivores as well as of domesticated sheep and cattle." The fact is that the cyanophoric glycosides (Burk’s Vitamin B-17) cause poisoning and death of these animals frequently. This is documented in the article by Professor Eric Conn (Exhibit 5), who states:

From the above it is clear why the ingestion of fresh, cyanophoric plant material by livestock can result in the death of the animal. Maceration by the animal of the fresh plant tissue as it is ingested initiates the enzymatic breakdown of the glycoside by the plant enzymes as described above. Therefore, the animal merely needs to eat enough of a plant that is sufficiently rich in cyanogen and enzymes to be poisoned. Members of the rose family (apples, mountain mahogany, choke cherries) have been cited for loss of much livestock in the United States; leaves of the eastern wild cherries may produce 200 mg KCN/100 g. According to Kingsbury, 1/4 lb of those leaves could kill a 100 lb. animal. Cyanophoric species of acacia have been
blamed for the death of sheep and cattle in Australia (9), South Africa (10) and the United States (8). In general, it was the leafy foliage of these plants that was consumed. It is common knowledge among farmers in the United States that their cattle must not be permitted to graze on young sorghum plants until "the cane is belly-high on the cow". The young sorghum leaves are particularly rich in dhurrin, and only in the older plants does the concentration become low enough to permit grazing. When the sorghum plant is taken for ensilage, the cellular breakdown and fermentation that occur in the silo release the HCN, which then escapes.

Dhurrin is a cyanogenic glycoside (a form of Vitamin B-17 according to Burk's definition), consisting of D-glucose, HCN and p-hydroxybenzaldehyde). It is quite similar to amygdalin. Dhurrin and amygdalin contain prussic acid (HCN).

The animals poisoned in the descriptions in the above paragraph were killed by what Burk calls "Vitamin B-17", acted upon by enzymes present in the same foods.

6. On page 10 of Exhibit A, Burk discusses the "nontoxicity" of laetrile. The toxicity of all substances depends on their dosage. It is well-known and well-documented that amygdalin presents problems of toxicity to human beings when it is consumed together with the enzyme beta glucosidase as in "apricot seed milkshakes". Under such circumstances, the enzyme liberates cyanide from amygdalin before the enzyme is destroyed by the gastric juice.

7. Also on page 10 of Exhibit A, Burk states that "meats, milk, cheese, eggs and other proteins may similarly produce cyanide when decomposed by suitable enzymes or catalysts". Meats, milk, cheese, and eggs are not proteins. They contain proteins and many other substances as well. Proteins do not produce cyanide when decomposed by enzymes. Burk has attempted to justify this statement by quoting a reference from the Journal of Biological Chemistry in 1913. The reference purported to show that cyanide was produced from various crude materials, including eggs and milk when it was fermented with Bacillus pyocyaneus. Such a procedure, fermentation by bacteria, leads
to synthesis of various substances, and does not represent liberation of such substances by an enzyme.

8. On page 11 of Exhibit A, Burk says that the body "can detoxify this cyanide with total bodily safety, usually forming the compound thiocyanate a normal constituent of blood". This is untrue. Thiocyanate at the concentrations formed from cyanogenic glycosides is a goitrogenic substance. Such substances are potential carcinogens. This is documented in the publications and research of Conn and Osuntokun (Exhibit 5).

9. On page 17 of Exhibit A, under the heading "Vitamin B-15 and Vitamin B-13", Burle states that both are "listed as such in the Merck Index". This listing does not make a substance a vitamin. The Merck Index compiles the literature. The publishers of the Merck Index have made the following statement: "The Merck Index has a strong medical character, but it must be emphasized that it is not intended as a therapeutic guide. Inclusion of a drug in this book is not to be taken as an endorsement but merely as a statement of the fact that such a drug exists."

While it is not involved in this proceeding let me state that pangamic acid is not a vitamin. The name "Vitamin B-15" for pangamic acid was apparently created by Mr. Ernst Krebs as a sales device for still another remedy.

Likewise, orotate or orotic acid also is not a vitamin. It is a compound formed in the body during the production of pyrimidines. It is readily and normally produced in the body from simpler substances. It also has not been possible to substantiate the claims for nutritional usefulness of orotic acid.

10. In conclusion, this pamphlet by Burk (his Exhibit A) contains no scientific evidence for his claim that "laetrile", "pangamic acid" and orotates are vitamins. Substantiation of such a claim would need demonstration in controlled and confirmed experiments of nutritional deficiencies produced.
by deprivation of each of these substances separately, and also the
prevention or cure of the specific deficiency by administering the "vitamin".
Such evidence is not on record in the scientific literature. It has not been
produced by Burk. Instead his pamphlet (privately printed and not subjected
to peer review) is a rhetorical and inaccurate piece of promotional literature.

B. Exhibit B: Excerpts from GRAS list. I have commented on this
above. The fact is that the substance on the GRAS list is free of cyanide.
The proponents of laetrile claim that the cyanide in laetrile is released
and acts selectively on malignant vis-a-vis normal cells. If laetrile contains
cyanide, it is not the substance on the GRAS list. If it does not contain
cyanide, the theory offered for its efficacy by those who attribute its
efficacy to cyanide release is by definition incorrect.

C. Exhibit C: This is a letter from Burk to Gregory Stout. The first
three paragraphs largely support what I've said, namely, that hydrocyanic
acid is liberated from amygdalin by enzymatic action. The fourth paragraph
is incorrect insofar as it states that the cyanide radical "can also be
released from many proteins in meat, eggs, milk, gelatin products, cottonseed
meal, peptones, etc. ..." The references to the Journal of Biological Chemistry
15:415-419, 1913, are to articles that described the production of hydrocyanic
acid not from proteins, but from the crude materials in paragraph 4 of Exhibit C.
Bacteria fermentations of crude substrates produced numerous substances by
synthesis. For example, the organisms, Bacillus pyocyaneus also produces the
toxic antibiotic, pyocyanin.

In the final sentence of Exhibit C, the GRAS list requirement is
incorrectly quoted. Amygdalin is not mentioned in the GRAS list.

D. Exhibit G: This purports to be a letter from Hans Nieper. The
vague assertions in it, for example, "bone marrow depression due to disease
can be controlled by amygdalin", are not supported by data. Similarly
statements such as "we observed that radiation by cobalt 60 apparently
enhances the effect of amygdalin and vice-versa”, have no support in data that the effect, if any, was not caused by cobalt 60. The second document in this exhibit is a manuscript by Nieper. The regimen described is incredibly complex, including as it does, BCG vaccine, C parvum, and bromelain, none of which are known to be effective or indicated in cancer. In addition, the unsupportable allegation is made that the enzymes of cell-bound immunity are strengthened by zinc orotate and carotene, or Vitamin A. Further, statements concerning the normalization of the intestinal flora by "old wives remedies" such as mucilaginous tea give me the impression that Hans E. Nieper, M.D., is at least unreliable (stronger words could well be applied). His statement that shellfish and sugar-rich foods are "cancer-inducing diets" is ridiculous.

The weird regimen detailed by Nieper including such items as application of carotene (up to 10 milligrams per liter in the form of carrot juice with cream) have traditional quackery characteristics. Nieper's manuscript tells us nothing. It provides no facts, figures, pathology and case histories. He contributes essentially nothing to science or these hearings.

E. Exhibit H: This is an article from the Journal of Applied Nutrition. This journal and the organization that publishes it are not recognized by the scientific community as being authoritative or sound. Standards are used in science, just as they are in the legal profession, and this organization simply does not meet these standards. This becomes evident in the "Editorial Comment on Dr. Krebs' Paper". Krebs is not a doctor. He is a promoter of laetrile.

In his publication, Krebs uses the term nitrillosides coined by him for beta-cyanophoric glycosides. These compounds are also known as "cyanogenic glycosides". They are of no dietetic significance except for their toxicity.

While most of the article is a repetition of claims that I have discussed earlier in this affidavit, a few comments are indicated because the article is replete with error.
For example, on page 80, Krebs stated that "Vitamin B-17" releases a specific and powerful cytotoxin "probably the most powerful one known". This is hydrogen cyanide. It is curious that Krebs admits that hydrogen cyanide is liberated by amygdalin while Burk has stated so vehemently that we don't have to worry about this. Again, in the second complete paragraph on page 81, Krebs states "there is no controversy, of course, on the fact that equimolar quantities of benzaldehyde and cyanide resulting from the hydrolysis of Vitamin B-17 will selectively kill cancer cells." (Emphasis supplied). This "fact" is non-existent. Vitamin B-17 is also non-existent.

On the bottom of page 81, the final paragraph carries the marginal statement: "No. Needs rewording and further qualifications". Presumably, this marginal note is in the handwriting of Dean Burk. In any case, the information in this paragraph is incorrect. Professor David Greenberg's article in Western Medicine, cited above and included in this administrative record as an exhibit to Professor Greenberg's affidavit, explains that there is no selective effect by malignant tissue on hydrolyzing amygdalin.

F. Exhibit I: Deposition by Raymond Ewell made in Austria, December 10, 1976.

1. In the second paragraph, Ewell states "anyone who claims that amygdalin is a toxic substance is indulging in sophistry or pseudo-science or has never examined the facts". However, Ewell does not point out the fact that amygdalin in foods and similar natural products occurs in association with beta-glucosidase which can hydrolyze it with the production of highly toxic hydrocyanic acid. Ewell then states "amygdalin has never been classified as GRAS or not as GRAS primarily because only a few people consume amygdalin in its pure form either as a food supplement or as a flavoring agent". This statement is correct, despite the fact that apparently Burk has written "NO" in the margin. Ewell then states "however,
many people in many parts of the world consume substantial amounts of amygdalin as a component of almonds, fruit seeds, buckwheat, tapioca, lima beans and many other foods". This is only partially correct. The cyanogenic glycosides present in tapioca and lima beans are not amygdalin. The corresponding compound, linamarin, present in lima beans is considered sufficiently hazardous that strains of lima beans high in this compound are excluded from the United States by the U.S. Department of Agriculture.

2. Ewell states that marzipan is "reportedly as high as 20% amygdalin". He is incorrect. The flavor and odor characteristic of marzipan are due to benzaldehyde, that is set free from amygdalin together with, hydrogen cyanide. The hydrogen cyanide is highly volatile and diffusable, and escapes.

3. On page 20, the analogy between amygdalin and sodium chloride (salt) is inappropriate. Hydrogen cyanide can readily be liberated from amygdalin by a common enzyme, but chlorine can be set free from sodium chloride only by the drastic and artificial process of electrolysis.

4. On page 2, paragraph 3, the statement regarding Vitamin B-12 is incorrect. Cyanide present in Vitamin B-12 is there unnaturally. It is derived from cyanide present in activated charcoal used during the refining process. Vitamin B-12 in its natural state as it occurs in foods such as liver, does not contain cyanide. Moreover, the cyanide present in commercial Vitamin B-12 is set free from the solution during exposure to light, and escapes without impairing the nutritional properties of Vitamin B-12.

5. Page 2, paragraph 3, is incorrect. Evidently Ewell is not familiar with the report of experiments with mice (Laster and Schabel, as cited above) showing that amygdalin was toxic when administered together with beta-glucosidase.

6. Page 2, paragraph 4, is incorrect in several ways. The illness reported by the California State Department of Health was characterized by the symptoms of cyanide poisoning. The cyanide was liberated from amygdalin
in the apricot kernels when milkshakes were prepared from these kernels by grinding them. Poisoning by analogous procedures has been repeatedly reported with apricot kernels and with bitter almonds.

7. Ewell's experiences with self-medication, and his personal beliefs, contribute very little to the scientific resolution of the matter of using amygdalin for the treatment of cancer.

G. Exhibit J: Undoubtedly many chemical companies supply amygdalin, and thousands of other chemical substances of both high and low toxicities. This does not make such substances "anti-cancer agents" as stated in the footnote.

H. Exhibit K: This is the affidavit of Professor Chauncey Leake. The eminence of Professor Leake as an authority on pharmacology and toxicology is unquestioned. His deposition avoids any mention of whether amygdalin is actually useful for any medical purpose. His reference to its clinical use are second hand and vague, perhaps intentionally so.

1. In paragraph 4 he states that "the seeds" (not specified, but references made to "bitter almonds, peach seeds, etc.") yield 0.25% of hydrocyanic acid, presumably by the action of emulsin. Emulsin is an obsolete name for beta-glucosidase. According to Professor Leake, 100 grams of the seeds would yield 0.25%, which is 250 milligrams, of hydrocyanic acid. This is a lethal dose. My previous explanation of the potentially toxic effect of amygdalin therefore receives confirmation by Professor Leake's deposition. He also states that "the oil of bitter almond because of its hydrocyanic acid has been employed in the coughs of phthisis and in the irritated coughs of children". It is obvious that the employment of hydrocyanic acid for this purpose would cause the coughs to be permanently stilled.

2. In paragraph 5 Professor Leake notes that five cases of cyanic (presumably cyanide) poisoning ... five occurred from eating bitter almonds or cherry or gum kernels. Dr. Ewell please note.
3. In paragraph 6 Professor Leake reports that amygdalin when used prior to 1938 was "safe when used in the treatment of cancer". However, he does not say whether it was effective. Nor does he state the form, dosage, purity, strength, route of administration, or other essential characteristics of what was reported to be amygdalin.

4. Paragraph 7. This recounts conversations with Dr. Ernst Krebs, without data, and the paragraph is pure hearsay.

5. Paragraph 8. Recites Professor Leake's opinion that amygdalin is safe and non-toxic when administered to humans and animals under commonly recommended dosages. However, he does not state what these recommended dosages are, for what purpose they are employed, or whether or not they are effective for any purpose.

I. Exhibit L: This is the affidavit of Charles Gurchot.

1. Paragraph 4 once again recognizes the liberation of cyanide from amygdalin in toxic form by enzymatic action.

2. Paragraph 5 discusses the 1845 report by Inosemtzeff. It contains nothing definite in the way of scientific information, as may well be expected from the date and origin of this report.

3. In paragraph 8 Gurchot states that he used amygdalin to treat cancer "around 40 years ago". He does not say whether the treatment was effective, nor does he describe the substance used in terms of its composition, purity, strength, chemical structure, or labeling.

4. Paragraph 11 notes a warning against using the preparation containing amygdalin for food. This warning is repeated in paragraph 12, and serves to counteract the cavalier way in which the ingestion of amygdalin has been recommended by Burk and others in this series of depositions.

5. In paragraph 14 Gurchot recites the use of amygdalin by various physicians at the University of California Medical School in San Francisco. The statement that it was recognized as "having some beneficial effects in the treatment of cancer" is not supported by documentation.
6. In paragraph 15 Gurchot states that amygdalin can be purchased commercially. Amygdalin is purchaseable as a chemical item. This has no bearing on the issues. Arsenic is also purchaseable.

7. Paragraph 16. This paragraph states that amygdalin was allegedly used for the treatment of cancer in California in 1934 and 1945. It is not possible to evaluate this statement. It is recognized that laetrile was not synthesized to its present form until well after 1945. The substance used between 1934 and 1945 may have been described as amygdalin, or may have contained amygdalin, but its composition, strength, purity, identity, and other essential characteristics are unknown.

28. I would like to comment on the statement by James Cason, dated March 13, 1977, submitted as part of this administrative rule making proceeding on laetrile.

A. The article that Cason appended to his letter is by Mr. Robert G. Houston, a person with no known qualifications in biochemistry who is with the Foundation for Mind Research, allegedly an organization in suburban New York. It is remarkable that Cason should have selected this inaccurate article for any use, including attachment to his deposition, when he could have furnished authoritative information on amygdalin by one of his own colleagues of great eminence in the field of cyanogenic glycosides, Professor Eric Conn, Department of Chemistry, University of California, Davis. I drew Dr. Cason's attention to Professor Conn's work in correspondence with him during the Spring of 1976.

Houston's article reports no original research by him, and I am not aware that Houston has published any original work on amygdalin. Professor James Manning, Rockefeller University, a well-known expert in sickle-cell hemoglobin, has shown that thiocyanate is ineffective in "unsickling"
hemoglobin S, the physico-chemical reaction that is needed for relieving the symptoms of sickle-cell anemia. Cason failed to mention that Houston's claims in this regard were rebutted in an article in the *American Journal of Clinical Nutrition*.

B. In paragraph 4 of his letter, Cason states that amygdalin is synonymous with "Vitamin B-17" which is incorrect, and has been repeatedly contradicted by authorities in nutrition. Cason lists garbanzo beans, bean sprouts, macadamia nuts, and alfalfa sprouts as "well known plants containing nitrilosides". The name "nitriloside" is not recognized among biochemists; it was coined by Mr. Ernst Krebs, the promoter of laetrile. In any case, the concentrations of cyanogenic glycosides present in such materials should be stated if the listing is to be of any significance. Lima beans also listed by Cason are grown from strains that have been selected to be low in cyanogenic glycosides, so as to minimize the possibility of cyanide toxicity occurring in consumers of such beans.

C. On page 2, line 10 of his letter, Cason states "it is widely recognized that people who will eat as much as 100 mg per day of nitrilosides rarely, usually never, become cancer victims." This statement is nonsense. There are no data supporting such a statement, and there are no data for the accompanying, similar, and untrue statement that "those who experience a low or negative incidence of cancer always eat diets high in nitrilosides". (Emphasis in original). This is a figment of Cason's fertile imagination.

The paragraph concludes with the statement that "the diets of the cancer-free population probably also contain considerable vitamin C". There are no "cancer-free populations". Certain forms of cancer, such as Burkitt's lymphoma, were discovered for the first time in African populations which Houston suggests are less prone to die of cancer.
D. On page 2 of his letter, Cason proceeds to construct a fantasy based on the false premise that there are cancer-free populations. Thiocyanate does not have essential functions in metabolism nor does it repress sickle-cell anemia crisis. On the contrary, it is a goitrogen, a substance that inhibits the activity of the thyroid gland and is, therefore, a potential carcinogen. The sentence beginning "This enzyme could develop ..." contains two conclusions based on false premises. The first false conclusion is rhodanese evolved because "the diet of the animal developing this enzyme had a constant low supply of cyanide, otherwise the enzyme would have nothing to work on". The enzyme has substrates that Cason doesn't mention. These are listed in the review on rhodanese by John Westley, Advances in Enzymology, Vol. 39. The second error is that rhodanese led to the surviving species. Cason suggests a self-serving and circular conclusion for the probable reality, which is that the enzyme, by changing cyanide to thiocyanate, would reduce the toxicity occurring due to exposure to cyanide. Cyanide is a far more deadly poison than thiocyanate even though thiocyanate is deleterious as indicated above, and as substantiated by scientific studies of African populations who are chronically exposed to cyanide poisoning by ingesting foods containing "nitrilosides" as Cason terms them (see Exhibit 5).

The final error is this paragraph is the last sentence, which states that malignant cells "do not have rhodanese, and are thus poisoned by cyanide. This wishful thought has been refuted by scientific data supplied by Professor David Greenberg, whose affidavit was submitted as part of the record.

E. On page 3, lines 7 and 8 Cason states that conventional therapy damages the prospect of successful treatment with laetrile, "especially if the victim's ability to fight stress and his will to live have been traumatically damaged by conventional cancer therapy". Conventional
cancer therapy does not "traumatically damage the ability of a patient to fight stress and his will to live". This sentence is derogatory, unjustifiable, cynical and slanderous. Conventional cancer therapy is designed to sustain the patient.

F. On page 3, Cason suggests that the Food and Drug Administration not prosecute violations of the Federal Food, Drug, and Cosmetic Act when violations include the prescription and administration of medications that have not been approved as new drugs. The FDA has a distinguished record in this field, particularly in stopping the use of cancer quack remedies. This is set forth in detail in Chapter 17 "The Most Heartless" of the book THE MEDICAL M'SSIAHS, by James Harvey Young (attached as Exhibit 6). This chapter starts with the quotation "Of the ghouls who feed on the bodies of the dead and dying, the cancer quacks are most vicious and most heartless".

Cason also implies that it is possible that the FDA is guilty of murdering with torture about 370,000 United States citizens per year. It is reprehensible that a university professor should engage in such hysterical innuendo. Cason then goes on to suggest that the public pocketbook be used to "establish that nitriloside therapy of cancer is worthless". In fact, the government has funded a series of experiments on laetrile which have shown it to be worthless. More important, however, is that if public money were spent in testing every quack cancer remedy that comes on the black market, the expenditure would rapidly reach billions. Furthermore, such a ridiculous procedure would be using human subjects as guinea pigs to satisfy the promoters of spurious remedies, and the physicians participating in such travesties of medicine would be subject (and rightly so) to malpractice suits.

G. Cason on page 3 states that "research on humans will be easy to accomplish". Obviously he has no idea of what is involved in experimenting on human subjects. For example, he states that amygdalin "can be safely
injected intravenously in amounts as large as can sugar (glucose sugar)." The long-term effects of injecting amygdalin are unknown. Foreign substances injected into the body can have delayed, pathological effects. There are some good warning signals of possibilities that might be encountered by prolonged injection of amygdalin: if, for example, amygdalin sets free cyanide in sufficient quantities there is a danger of causing blindness. If the injections also resulted in the formation of thiocyanate, this could cause goiter.

H. Cason also asserts on page 3 that the FDA has "employed all the resources at their command, supported by taxpayers dollars, to prevent gathering of clear evidence as to whether amygdalin is effective in cancer therapy" (emphasis in original). This statement is patently false.

I. In the penultimate paragraph on page 3, Cason reiterates that the FDA has prevented "the assemblage of evidence concerning the worth of the nitrilosesides therapy of cancer." This charge is false. The FDA has collaborated with the National Cancer Institute in an assiduous effort to find evidence of the effects of amygdalin in cancer therapy. No evidence of Laetrile's worth has been forthcoming.

J. Cason's concluding "simple thoughts" have nothing to do with the matter at hand. If he wishes to eat apricot seeds and ascorbic acid he is perfectly free to do so and the FDA will let him. If Cason wants to eat thistles, pine cones, and live snakes, the FDA will not interfere with him. The issue is whether Laetrile should be sold for the treatment of cancer. It is an issue of money, fraudulence and public health policy.

29. Cason's statement is accompanied by a three page dissertation distributed by him to Chemistry 3B, an undergraduate course in organic chemistry at the University of California, Berkeley, in Winter Quarter, 1975.

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I have the following comments with respect to this handout.

A. It is a promotional piece for the article by Houston. As an example of Cason's evaluation of Houston's article, he points out that it carries 121 references. However, he does not state which of these references have any meaning in terms of Houston's claims.

B. Cason starts off with accepting Houston's false thesis that cyanate can be produced from thiocyanate in the body. This conversion does not take place. Cason states in his first paragraph that a nitriloside is "commonly called laetrile or vitamin B-17 in medical practice". There is no such thing as vitamin B-17.

C. In his next paragraph Cason speaks of the "cancer industry". No such industry exists. The term was evidently used with the intent of being a slur.

D. On page 2, Cason draws a false inference that the fact that cyanide is converted to thiocyanate implies that thiocyanate has "some functions in metabolism". This is not the case. It is much more probable that the conversion of cyanide to thiocyanate is an evolutionary adaptation -- a detoxification mechanism -- to change the intensely poisonous cyanide into the far less toxic substance, thiocyanate.

E. In his next paragraph, Cason attempts some arithmetic. His arithmetic is erroneous. He says that a minimum of 65 apricot kernels would be needed to produce poisoning. However, in CALIFORNIA MORBIDITY, a case of cyanide poisoning was reported which occurred in a man who had eaten "approximately 48 seeds, of apricots". The well-known standard textbook TOXICANTS OCCURRING NATURALLY IN FOODS, 2nd Edition, published by the National Academy of Sciences, states on page 450 that a three year old girl incurred cyanide poisoning from eating approximately 15 apricot kernels. It is incredible that Cason should not have furnished standard reference material on the subject to his students, but instead supplied them only with the useless article by Houston.
F. Cason says "it should be mentioned that hydrogen cyanide is much less toxic than certain other normal regulatory components in humans". (Emphasis added). Hydrogen cyanide is not a "normal regulatory component". It is a deadly poison, according to the Merck Index, and the lethal dose (not the LD50) is listed at 1.6 milligrams per kilo of body weight for dogs.

G. On page 3, Cason states "there appears to be no case on record of fatal poisoning of a human from apricot kernels, bitter almonds, peach kernels." It is incredible that a professor of chemistry should perpetrate such a falsehood. Anyone interested in finding the facts could easily refer to readily available literature. For example:

A fatal case of cyanide poisoning following the ingestion of bitter almonds, which contained the cyanogenic glycoside, amygdalin was reported once before, and a comment on the surprisingly large number of such cases was made at that time.


H. Ironically Cason finishes this document with a correct statement. "Don’t ever turn the cattle into the millet until the grass is at the cow’s belly." This is because farm livestock are often poisoned by cyanogenic glycosides, resulting not from the presence of bacteria in the first stomach of ruminants, but because plant materials contain beta-glucosidases.

30. I would like to offer the following comments on the letter from Harold W. Manner to the Hearing Clerk, dated March 22, 1977: Manner says that laetrile and amygdalin are not synonymous. This is incorrect. Lætir is not a contraction for the "chemical levo-mandelonitrile". The compound mandelonitrile is formed from amygdalin (laetrile) by the action of the enzyme beta-glucosidase, but this action does not take place in the body.
The amygdalin of illicit commerce is not racemic. On the first complete page of his manuscript, Manner states that Laster and Schabel used the racemic form of amygdalin. This is incorrect. Laster and Schabel state that they used "d-mandelonitrile gentiobioside; laetrile". This is not the racemic form. Wodinsky and Swiniarski used the same compounds as Laster and Schabel. So did Hill and co-workers, who specifically state that the compound they used was "a naturally occurring cyanoglucoside which is found in many plant products". The conclusions drawn under "Results and Discussion" by Manner are therefore incorrect because of his foolish error in nomenclature.

In any case, the results are not novel, and contribute nothing to the question of the effect of amygdalin on cancer.

31. In summary, I would like to state the following facts:

A. The name laetrile is currently applied to amygdalin, a cyanogenic glycoside present in apricot seeds and in seeds of other members of the rose family. Amygdalin is 2 molecules of glucose combined with 1 molecule of cyanide and 1 molecule of benzaldehyde.

B. The cyanide in amygdalin is inert, but it is released as hydrocyanic acid (HCN, prussic acid, hydrogen cyanide) by an enzyme system, containing beta-glucosidase. This enzyme system is present in apricot seeds, bitter almonds, and leaves of various plants.

C. Amygdalin, under the name laetrile, is advocated by certain individuals for the treatment of cancer. There is no scientific support for its use for this purpose. All attempts to substantiate the alleged usefulness of laetrile in preventing, curing, or reducing the growth of cancerous tumors have failed. This conclusion is supported by all leading authorities such as those in the National Cancer Institute.

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D. The failure of the proponents of "laetrile" to secure evidence for its effectiveness in cancer chemotherapy has been followed by their attempt to create a vitamin role for amygdalin and its related cyanogenetic glycosides such as linamarin, which is present in lima beans and cassava. Not a single shred of experimental evidence exists for support of such a claim. Amygdalin has no vitamin-like action. It is a toxicant present in natural foods, and is recognized and classified as such in the National Academy of Sciences book on the subject.

E. Chronic toxicity caused by cyanide is well known among consumers of linamarin as occurring in cassava. The symptoms are those of tropical ataxic neuropathy, often ending in blindness. This is common in West Africa. A second effect is goiter resulting from the cyanide being converted to thiocyanate enzymatically in the body. Thyroid cancer can be caused as a terminal effect of goiter.

F. Amygdalin (laetrile) is not a food, because it does not supply a nutritionally beneficial effect.

G. Nothing is known of the long-term effects of amygdalin when injected.

H. The ban on interstate shipment of amygdalin (laetrile) as a drug or an article of food should be continued by the United States Food and Drug Administration.

I. Although it is not feasible to prohibit the eating of apricot seeds, bitter almonds, and other natural products containing amygdalin, the public should be warned against the practice, because it has resulted in a substantial number of cases of poisoning and some deaths.

J. The promotion of laetrile includes false statements that cancer is a deficiency disease caused by lack of "vitamin E-17" (amygdalin) in a manner analogous to the occurrence of scurvy from a lack of vitamin C. Such statements deceive gullible people in a manner that is similar to previous "cancer hoaxes", and the perpetrators of such frauds have been
well characterized as "the most vicious and most heartless" of all those who exploit desperate and sick people.

Thomas H. Jukes, Ph.D.

Subscribed and sworn to before me by the said Thomas H. Jukes, Ph.D., this 19th day of April, 1977.

[Signature]

Notary Public
My Commission Expires: July 1, 1978
BIOGRAPHICAL SKETCH

Thomas Hughes Jukes, Ph.D., D. Sc.


Current Position: Professor-in-Residence, Medical Physics and Research Biochemist, Space Sciences Laboratory, University of California, Berkeley, California 94720.

Fields of Research: Vitamin B complex, especially riboflavin, nicotinic acid, pantothenic acid, vitamin B_6, choline, folic acid, vitamin B_12; folic acid antagonists in cancer chemotherapy, antibiotics in nutrition, nutritional deficiencies, amino acid code, protein chemistry, molecular evolution, non-Darwinian evolution.

Author: B-vitamins for Blood Formation (book); Antibiotics in Nutrition (book); Molecules and Evolution (book); more than 250 articles in scientific journals.

Member: American Society of Biological Chemists; American Institute of Nutrition (Council, 1941-46; Fellow, 1973); American Chemical Society; American Society of Animal Science; Society for Experimental Biology and Medicine (Editorial Board, 1953-58); Biophysical Society.


Non-scientific Memberships: Sierra Club, American Alpine Club (Council, 1960-63); Explorers Club, Faculty Club (Berkeley), Trustees for Conservation (San Francisco, President, 1970-71), Hat-Chat Club (San Francisco).

Other Information:orden Award in Poultry Nutrition (1947); elected to honorary Life Membership in American Society of Animal Science (1961).
Laetrile for Cancer

Thomas H. Jukes, PhD

Another chapter is being written in the melancholy history of cancer quackery. This chapter, entitled "Laetrile," follows the outline of its predecessors. First, a remedy is introduced resulting from a novel "strange idea." Next, its promoters become so dedicated to advocating the remedy that they cannot retreat from a position which becomes untenable as a result of exposure of the worthlessness of the remedy. Third, the promoters are reinforced in their fraudulence by champions of the "underdog" against the "establishment," and by the surviving relatives of the deceased victims of cancer. These relatives, believing that treatment with the remedy was the best possible therapy. Finally, vast sums of money and amounts of time are wasted on elaborate tests of the "remedy" by qualified scientists who should be doing something useful. These tests are usually undertaken because of coercion by legislators and other governmental officials who respond to letters from voters—letters that are often generated by the "health food" press.

The substance, laetrile, or as properly named, amygdalin, is a cyanogenetic glycoside found in seeds of apricots, peaches, and plums. Such glycosides are toxicants occurring naturally in foods. Similar compounds are in vetches, clovers, sorghums, cassava, lima beans, and acacias. They are characterized by hydrolysis by enzymes (β-glycosidases) to yield a sugar, usually dextrose, and a second component, mandelonitrile, which consists of a molecule of hydrogen cyanide combined with a molecule of benzaldehyde. This component decomposes into benzaldehyde and cyanide, either spontaneously or by the action of a second enzyme. The cyanogenic glycosides have no food value or vitamin activity, although the misnomer, vitamin B₁₂, is used in the promotion of laetrile. Indeed, in cultures where the consumption of cyanide-poisoning occurs in human beings as a direct result. This has been described in Nigeria in patients who subsist on cassava diets. Cassava farmers and processors appear to have the highest risks for development of the disease, according to Osuntokun. He described the disease as tropical ataxic neuropathy, attributable to chronic cyanide intoxication. The symptoms include lesions of the skin, mucous membranes, optic and auditory nerves, spinal cord, and peripheral nerves.

Claims

The use of laetrile to treat cancer was originally based on a proposal by Ernst Krebs, MD, that the substance would be broken down by an enzyme in cancerous tissue to liberate cyanide, which would "kill the cancer." This wishful concept was destroyed by the following facts: (1) there are only traces of β-glucosidase in animal tissues and even less in experimental tumors, and (2) cyanide diffuses rapidly and would poison the surrounding normal tissues, or be transported to cause systemic poisoning.

The proponents of laetrile then changed their strategy. Their next claim was that amygdalin was hydrolyzed to mandelonitrile, which was carried to the liver and converted to the β-glucuronide. This alleged compound was asserted to be carried to the cancer tissue, where it was said to be hydrolyzed by an enzyme, β-glucuronidase, with the subsequent liberation of cyanide. There was no basis for such a claim.

The sponsors of laetrile made an application to the Food and Drug Administration (FDA) through an "Investigational and New Drug Application." Their application was reviewed and rejected because of insufficient scientific evidence that the product was safe and effective in the treatment of cancer. For the review, FDA convened an outside committee of cancer experts to review all submissions. They also rejected the evidence as totally inadequate. But the sponsors of laetrile, faced with a roadblock, proceeded to "run an end run." Since their compound had been ruled out as a drug, they decided...
to transform it into a vitamin, thus making it a food rather than a drug. They hoped that this transformation would release laetrile for shipment in interstate commerce as "vitamin B17." Of course, laetrile and its relative, prunasin, have not the slightest resemblance to a vitamin. The crucial property of a vitamin is that its absence from the diet produces a specific deficiency disease in vertebrate animals. The cyanogenic glycosides do not have this property.

Judicial Findings

Laetrile, under the generic (and correct) name of amygdalin is sold as a laboratory chemical in the United States. Large quantities are smuggled from Mexico for distribution through "health food" channels. Its use for cancer treatment is illegal under federal regulations and is also prohibited by law in many states. Crude preparations of laetrile from apricot and peach kernels have been marketed under such names as "Bee-17" and "Aprikern." A trial was held in California, April 22, 1975, of the case of the United States (plaintiff) vs General Research Laboratories inc (defendant). The decision of the court was based on 42 findings of facts. Among them were the following:

1. Because of its hydrogen cyanide content, Aprikern is unfit for food.
2. Vitamin B17 is also commonly known as amygdalin and laetrile.
3. There is no vitamin B17 that is a recognized vitamin in human nutrition.
4. There is no regulation in effect permitting the use of amygdalin in foods as a food additive or exempting amygdalin from the food additive requirements of the Federal Food, Drug, and Cosmetic Act.
5. The danger in the use of remedies such as vitamin B17, also known as amygdalin and laetrile, in the treatment, prevention, cure, and mitigation of cancer is in delaying or omitting diagnosis and treatment that is generally recognized by the medical profession as beneficial and effective.

The judge found that Bee-17 and Aprikern are foods and also drugs under the Federal Food, Drug, and Cosmetic Act. He found that both products are adulterated foods, misbranded as both foods and drugs. His decision placed General Research Laboratories inc under permanent injunction on April 21, 1975.

Despite this decision, the proponents of laetrile are infinitely ingenious, and a large revenue is undoubtedly derived from its sale. They have enlisted the support of a scientist, Dean Burk, Ph.D, formerly of the National Cancer Institute, who has excellent scientific training and background. Dr Burk mistakenly asserts that laetrile is a vitamin, "vitamin B17." He also erroneously asserts that it is "almost impossible...ever to declare scientifically that a given compound is not a vitamin," and that "meats, milk, cheese, eggs, and other proteins [sic] may similarly produce cyanide when decomposed by enzymes or catalysts." Cyanide cannot be produced by the enzymatic splitting of proteins. Dr Burk has compounded his error by asserting the existence of "vitamin B17," and "vitamin B17." These vitamins do not exist; "vitamin B17" is an inert compound (orotic acid) and "vitamin B17" is another product of the imagination of Mr Ernst Krebs, Jr, the leading proponent of laetrile. When Dr Burk was confronted with the fact that his former professor and mentor, David Greenberg, Ph.D, had exploded these erroneous claims, Dr Burk responded that he could not understand how Dr Greenberg had made such a mistake. But the shoe is on the other foot. The Committee on Nomenclature of the American Institute of Nutrition "finds no scientific evidence for the existence of a 'nutritive' identified as vitamin B17..." This terminology is neither recognized nor used by qualified nutritionists. "The Committee...finds no scientific evidence that Laetrile has nutritive properties or is in any way of nutritional value for either animals or humans."

Sponsored Studies

The sellers of laetrile argue that it has been found active against cancer in mice by Dr Sugirua at the Sloan-Kettering Institute. The background of Sugiura's test is as follows: In 1972 and 1973, petitions said to be signed by 43,000 people were sent to President Nixon. The petitions demanded that the anticancer properties of laetrile be tested experimentally. Four studies with animals were set up: two by the National Cancer Institute, one at Sloan-Kettering Institute, and one at the Catholic Medical Center in Queens, New York. The studies sponsored by the National Cancer Institute under contract were with mice. No anticancer activity was found in any of the systems tested. The studies at Sloan-Kettering Institute were carried out by Sugirua. In a preliminary unpublished report, Sugirua stated that 72% of the mice in central groups had lung metastases, while metastases developed in only 17% of those treated with laetrile. This report was "leaked" to laetrile proponents who gave it wide publicity. However, negative results were obtained in a collaborative experiment carried out by Sugirua and Daniel Martin of the Catholic Medical Center. There was no difference between mice treated with laetrile and the controls in the lungs from the mice that were bioassayed by transplanting into fresh animals to see whether tumors would grow. Two other studies at the Sloan-Kettering Institute were negative. Dr Martin is quoted (Medical World News Oct 6, 1975) as saying: "I flatly and categorically tell you that laetrile is without activity against spontaneous tumors in mice—period."

Further Findings

Amygdalin may be refined from raw materials so that it is free from beta-glycosidase. However, if foods containing this enzyme are simultaneously eaten, cyanide will form, as in the case of cyanide poisoning in a three-year old girl who had eaten 15 apricot kernels. Several cases of cyanide poisoning from apricot kernels were recently summarized by the California State Department of Health. The victims had purchased the kernels as "health foods." Typically, they were rushed to the emergency rooms of hospitals, where vomiting was induced, and they recovered as reported in California Mornings (Sept 1, 1975; Nov 14, 1975; Dec 26, 1975).

One of laetrile's closest chemical relatives, the glycoside lizaradin, that is present in cassava, causes hundreds of thousands of people to live in a state of chronic poisoning that frequently results in blindness, in Africa, Jamaica, and Malaysia.
Subtoxic amounts of cyanide are converted in vivo to thiocyanate, which is goitrogenic. Osuntokun reported that patients with atoxic neuropathy associated with eating cassava had a higher prevalence of goiter (2% to 5%) than the general population. All goitrogens are potentially carcinogenic; this was the reason for the "cranberry incident" in 1959, in which cranberries were condemned by the Department of Health, Education and Welfare for containing traces of a goitrogenic weed-killer. Laetrile is therefore a possible carcinogen.

On Dec 16, 1975, a superior court jury returned guilty verdicts after a four-month trial in which five persons were charged with conspiring to sell laetrile as a cancer cure. On Dec 23, 1975, three persons were arraigned in US magistrate's court in San Francisco on charges of smuggling an estimated $200,000 worth of laetrile into the United States.

The California State Department of Health states: Under the current program of deception, lists of "nutrition oriented" doctors are provided the patient to visit with their cancer problems. In order to avoid prosecution, the practitioners disclaim any intent of treating cancer. Instead they pretend to offer nutritional therapy as a treatment for the "nutritional deficiency" or the "nitrosidine deficiency disease" which they allege the patient has. Treatment consists of excessively large doses of the known vitamins as well as the intravenous administration of "vitamin B_{12}.

Legislation has been introduced into the California Assembly, at the request of the National Health Federation, to prohibit regulation of the "right of "healing arts practitioners" to use "diet, foods, components of foods, herbs, prayer or harmless devices" ... as a remedy for any disease ... " The bills would remove the Department of Health's current regulations on laetrile.

One would think that with the disappearance of the various fantasies surrounding laetrile, the justification for promoting it would vanish. But mythology is more persistent than velocity. Although the song has ended, the melody lingers on, becoming even more strident; laetrile, no longer claimed to be a "magic bullet" that destroys cancer cells with cyanide, has become transmuted into the fake "vitamin B_{12}.

References

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FCTXAV 11(1) 1-174 (1973)
CYANIDE POISONING FROM THE INGESTION OF APRICOT KERNELS

An incident of possible cyanide poisoning in two health food faddists who consumed apricot kernels was recently reported from Los Angeles. A man and his wife purchased a two-pound bag of apricot kernels at a local health food store. They stored the kernels with dried apricots in distilled water overnight and the following day pureed the ingredients in a blender. The reconstitution was bitter and took some effort to swallow. About an hour after drinking the mixture, the wife complained of the discomfiture, tachycardia and feeling strange. She drank some water and vomited. Within minutes of his wife’s onset, the husband became symptomatic also and complained of headache, light-headedness, tachycardia, a generally strange sensation, and in vision...“as if looking through frosted glass.” He felt impending doom.

They were rushed to the emergency room of a nearby hospital. Vomiting was successfully induced, and after several hours of observation, they were released. For the next three days the husband complained of insomnia and tininess. The wife had died which surprised in one day. Both recovered fully.

In apricot kernels, apple seeds, cherry and peach pits, as well as the pits and seeds of some other fruits, there is a cyanogenic glycoside called amygdalin. This substance may liberate hydrogen cyanide and produce the characteristic odor of bitter almond. Symptoms may develop within an hour of ingestion, and include dyspnea, asphyxia, cyanosis, vomiting, lassitude, prostration, twitching, convulsions, stupor, paralysis, coma and in some cases death. Chronic cyanide intoxication has hypothetically been cited as a cause of some of the neuropathies seen in developing countries where cyanogenetic seeds and nuts are consumed. He had also eaten a few kernels separately, for a total consumption of approximately 48 seeds.

Cyano-induced vomiting was induced in both by specious and the husband. The symptoms rapidly subsided. Fragments of kernels were observed in the vomitus of both. The wife was asymptomatic. Apricot kernels, along with cherry and peach pits and apple seeds and other pits and seeds, contain a cyanogen glycoside called amygdalin, which releases hydrogen cyanide upon reaction with digestive enzymes. Symptoms of cyanide poisoning develop soon after ingestion, including dyspnea, cyanosis, vomiting, prostration, excitement, convulsions, stupor, paralysis; sometimes death, depending on dosage. The minimum number of seeds needed to cause death or death is not known. Any of apricot kernels (especially when crushed) can remove the cyanide, but this requires up to ten hours.

Chronic cyanide intoxication has been postulated as a cause of neuropathies in some developing countries where cyanogenetic seeds and nuts are consumed. The Cyanide Poisoning from ingestion of apricot kernels was reported in California Morbidity on September 1, 1972.

COMMENT: Apricot kernels and similar pits and seeds and related products are widely promoted as having disease preventivc, curative, and prophylactic properties and sold at health food stores. Physicians should be aware of the possibility of cyanide poisoning when eating such products are consumed.


*Case reported by William A. Townsend, M.D., Chief, Division of Medical Services, San Diego County.

CYANIDE POISONING FROM APRICOT KERNELS

On October 22, 1975, a 34-year-old man residing in San Diego County developed symptoms of cyanide poisoning from ingestion of apricot kernels. A one-pound package of raw, dried apricot kernels was purchased at a health food store as part of the preparation of milk shakes, following a recipe in the magazine Prevention. The kernels were roasted at 300°F for 10 min and 48 kernels were used, together with milk and honey, to prepare two milk shakes. The man’s wife consumed only a small amount of her milk shake since she didn’t like the taste, and the man drank all of his milk shake plus the remainder of his wife’s shake. He had also eaten a few kernels separately, for a total consumption of approximately 48 seeds.

Around one hour later the husband developed forceful vomiting, headache, flushing, heavy perspiration, distress and faint. The couple immediately went to a local emergency room where vomiting was induced in both by specious and the husband. The symptoms rapidly subsided. Fragments of kernels were observed in the vomitus of both. The wife was asymptomatic.

Apricot kernels, along with cherry and peach pits and apple seeds and other pits and seeds, contain a cyanogen glycoside called amygdalin, which releases hydrogen cyanide upon reaction with digestive enzymes. Symptoms of cyanide poisoning develop soon after ingestion, including dyspnea, cyanosis, vomiting, prostration, excitement, convulsions, stupor, paralysis; sometimes death, depending on dosage. The minimum number of seeds needed to cause death is not known. Any of apricot kernels (especially when crushed) can remove the cyanide, but this requires up to ten hours.

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The cyanogenetic glycosides are compounds that yield hydrogen cyanide (HCN) upon treatment with acid or appropriate hydrolytic enzymes. These compounds have a wide distribution among the higher plants, but they are also found in ferns, moths, and insects. More than 1,000 species of plants are reported to be cyanophoric; that is, HCN is released when tissues of the plant are crushed or otherwise disrupted. Although the production of HCN is usually attributed to the presence in the plant of one or more of the 20 known glycosides of α-hydroxynitriles (cyanohydrins), the parent glycoside has been positively identified in fewer than 50 species. The cyanogenetic glycosides have been the subject of recent reviews.1,2

Table 1 lists several of the more common cyanogenetic glycosides, some plants in which they occur, and the products formed on hydrolysis. The well-known toxicity of these compounds is due to the production of HCN, a potent respiratory inhibitor. The site of inhibition is the enzyme cytochrome oxidase, the terminal respiratory catalyst of aerobic organisms. Also usually produced on decomposition of a cyanogenetic glycoside is an aldehyde or ketone with which the HCN was combined as a cyano hydrin (Figure 1). The glycosides may contain as their sugar

* Literature reviewed to November 1971.
component a monosaccharide (usually glucose) or disaccharides such as vicinal and gentiobiose. The carbon atom to which the glycosyl moiety is attached may be asymmetric and provide the possibility of two dia stereoisomeric forms yielding the same products on hydrolysis (e.g., prunasin and sambunigrin, dhurrin and taxiphyllin).

Table 1 also shows that there is no obvious pattern in the distribution of cyanogenetic glycosides in nature. There is a fairly common occurrence in the rose family of two of the five cyanogens that produce benzaldehyde on hydrolysis. A third, sambunigrin, is also found in several legumes; they are not restricted to that family. It is unwise to generalize regarding which parts of a cyanophoric plant contain the cyanogenetic glycoside; they have been found in roots, tubers, stems, leaves, flowers, and seeds. Seeds of a cyanophoric species may not necessarily contain the glycoside, however. For example, sorghum seed with its high starch content can be safely consumed as food because it is lacking or very low in cyanogen. On germination, however, the dark-grown sorghum seedling may reach a concentration of 0.3-0.5% HCN (dry weight) within a period of 3 or 4 days, and young, green leaves are a rich source of dhurrin.

Knowledge of the manner in which cyanogenetic glycosides give rise to HCN permits one to better understand some of the information that is available on poisoning by these substances. The action of two enzymes usually found in plants that contain cyanogenetic glycosides is illustrated in Figure 1 for linamarin, a cyanogen occurring in cassava (Manihot sp.), and dhurrin, a cyanogen in plants of the Phascolus genus. The initial reaction involves the hydrolysis by the β-glycosidase of the β-glycosidic bond between the sugar and the aglycone (in this case, 2-hydroxyisobutyronitrile or acetone cyanohydrin) of the glycoside. In the reaction, the aglycone differs from the α-glycosides (amygdalin) of the mammalian digestive tract that hydrolyze only α-glycosidic bonds.

![Cyanogenetic Glycosides](image)

**FIGURE 1** The decomposition of linamarin by plant enzymes. In reaction (a), linamarin (2-(D-glucopyranosyloxy)isobutyronitrile) is hydrolyzed by the β-glycosidase linamarase to form β-D-glucopyranoside (I) and 2-hydroxyisobutyrogenitrile or acetone cyanohydrin (II). In reaction (b), the dissociation of the cyanohydrin to HCN and acetone (IV) is catalyzed by a hydroxynitrilase.

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Although the α-hydroxynitriles (cyanohydrins) produced by the action of plant glycosidases will dissociate nonenzymatically, hydroxy­nitrile-lases that catalyze the dissociation of these compounds are present in cyanophoric plants. In the presence of the lyase, the cyanohydrin dissociates to produce HCN and the product ketone (or aldehyde). While an enzyme catalyzing the dissociation of acetone cyanohydrin (Figure 1) has not been studied in a higher plant, such an enzyme has been reported in a fungus. The hydroxynitrile lyases of almonds and sorghum have been extensively examined.

The literature on cyanogenesis occasionally refers to the "HCN content" of a plant or plant tissue. It should be emphasized, however, that the HCN produced, according to Figure 1, only after disruption of the plant cell has occurred. Presumably in the intact plant the degradative enzymes are spatially separated from the cyanogenetic glycoside. Moreover, little, if any, free HCN would be expected to accumulate in the cell since, being volatile, it would escape to the atmosphere. HCN is also actively metabolized by many plants, the nitrile group being converted to the amide group of asparagine.

From the above it is clear why the ingestion of fresh, cyanophoric plant material by livestock can result in the death of the animal. Maceration by the animal of the fresh plant tissue as it is ingested initiates the enzymatic breakdown of the glycoside by the plant enzymes described above. Therefore, the animal merely needs to eat enough of a plant that is sufficiently rich in cyanogen and enzymes to be poisoned. Members of the rose family raffles, mountain mahogany, choke cherries have been cited for loss of much livestock in the United States: leaves of the eastern wild cherries may produce 200 mg HCN/100 g. According to Kingsbury, 1.4 lb of those leaves could kill a 100-lb animal. Cyanophoric species of acacias have been blamed for the death of sheep and cattle in Australia, South Africa, and the United States. In general, it was the leafy foliage of these plants that was consumed. It is common knowledge among farmers in the United States that their cattle must not be permitted to graze on young sorghum plants until "the cane is really high on the cow." The young sorghum leaves are particularly rich in dihydroxynitride, and only in the older plants does the concentration become low enough to permit grazing. When the sorghum plant is taken for ensilage, the cellular breakdown and fermentation that occur in the silo release the HCN, which then escapes.

Several methods are available for determining both the presence and the amount of cyanogenetic glycosides in plants. These are based on maceration and extraction of the tissue with a buffer or \( \text{H}_2 \text{O} \), followed by hydrolysis by the enzymes that are usually present in the

\[ \text{CN} + \text{S}_2 \text{O}_3^2- \rightarrow \text{CNS}^- + \text{SO}_3^- \]

Rhenadase, the enzyme that catalyzes this reaction, is widely distributed in animal tissues. The thiocyante produced is excreted in the urine. While the conversion of cyanide to thiocyanate represents a detoxification of the HCN, it should be noted that thiocyanate in turn is a goitrogenic agent. (See Chapter 10, p. 219.)

The accidental poisoning of humans who ate bitter almonds or the pits of peaches or apricots is recorded. There is one case of poisoning...
of children who had eaten large amounts of western choke cherries without removing the stones.14 These instances of human poisoning are similar to those involving livestock in that the fresh plant material provides both the cyanogenic glycoside and the enzymes responsible for the production of the lethal HCN. If the enzyme had been totally lacking in these plants, one might think that modest amounts of the intact glycoside could be safely ingested, for mammals do not appear to contain digestive enzymes that hydrolyze β-glycosidic bonds. There are, however, conflicting reports regarding the toxicity of purified glycosides administered orally to experimental animals.5-19

The occurrence of cyanogenic glycosides in plants (Table 1) that are commonly taken by man as food can result in acute cyanide poisoning. In some instances the poisoning occurred with cooked plant material, suggesting that care was not taken to remove HCN released during soaking and prior to cooking of the plant. In a review on the medical significance of cyanogenic glycosides in plants, Montgomery21 has cited numerous references to the poisoning of humans by cassava and lima beans. The sweet potato or yam, maize, bamba, chick pea, and sorghum are also mentioned as food plants capable of producing HCN. Viehöver22 has documented numerous cases of poisonings by lima beans, a species that is widely distributed in the world and one of the important edible legumes.

The HCN-producing capacity of lima beans is known to vary, with native American strains containing less than those originating in the east.22,23 While a white American variety produced only 10 mg HCN/100 g of seed, a white Burma variety yielded 200 mg, and a black Puerto Rican variety produced 300 mg HCN/100 g of seed. Since the lethal dose of HCN for the adult human is in the range of 50-250 mg, 100 g of seed of the wrong variety could easily prove fatal. In some areas where legumes are a staple of the diet, the daily intake may reach 200-300 g of beans.24 Today, the importation of lima beans is restricted by several countries, including the United States, to varieties yielding less than 20 mg HCN/100 g of seed. Selective breeding of low-cyanide varieties has also been encouraged.

The toxicity of cassava has long been recognized.21,22 However, it remains an important food plant because the peoples employing it have developed means of preparation that serve to remove or hydrolyze the linamarin and lotaustralin and to destroy the β-glucosidase that is present. Thus, the cassava, which is rich in starch, is scraped or grated, then soaked in water, and allowed to "ferment" for several days. Under these conditions, the cyanogen is extensively hydrolyzed, and both it and its dehydration products leached out. The soaked plant tissue is then dried, pounded into a flour, and, depending on the local traditions, made into cassava bread or boiled into a paste. Obviously such procedures can greatly reduce the cyanogen content of this important food, but Osuntokun24 cites the following figures as evidence that certain preparations of cassava common in Nigeria can still remain a source of cyanide and result in chronic cyanide poisoning. Osuntokun states that the amount of HCN released from fresh cassava root (38 mg/100 g) is reduced to 1.1 mg HCN/100 g in a cassava preparation known as "gari." Another preparation known as "purpuru," which is not as extensively washed, can yield 4-6 mg HCN/100 g of cassava. Some Nigerians may consume 750 g of cassava per day; this corresponds to 8 mg of HCN if the food is taken as "gari." This amount, however, would increase to 32-48 mg HCN if "purpuru" is eaten. These values, which approach the lower limits of the lethal dose of HCN (35 mg) cited earlier, represent HCN that can be released by further enzymatic hydrolysis, distillation, and determination. Whether all of the "available" HCN in this preparation would be released in the consumer is doubtful, unless, as frequently suggested, the bacteria of the lower digestive tract can degrade the cyanogenic glycoside.

In a series of reports, Osuntokun and co-workers have described recent evidence linking the degenerative disease known as tropical ataxic neuropathy to chronic cyanide intoxication of dietary origin.24-27 These papers implicate the high consumption of cassava in the disease in a group of Nigerians. The subjects exhibited an increased level of thiocyanate in the plasma and an increased excretion of this compound in the urine. Since thiocyanate is the compound formed when cyanide is detoxified in the animal body,28 an increased cyanide intake was indicated in these patients. Moreover, these individuals exhibited higher levels of plasma cyanide (free and bound) than controls.28

Montgomery, in reviewing the question of chronic cyanide poisoning, points out21 that tropical amblyopia (blindness) is common in West Africa. He cites others who proposed that cyanide in cassava was the cause. Related neuropathies have been described in Jamaica and Malaya, where cassava is consumed. A diet of millet (sorghum) consumed while Senegalese may be responsible for a syndrome similar to ataxic neuropathy.29 Some prisoners of war subsisting on a diet composed mainly of rice, cassava, sweet potato, and mung beans developed amblyopia.21 While chronic cyanide toxicity may be a major factor in each of these conditions, attention must be paid to the possibility of dietary imbalance, which may increase an individual's susceptibility to trace amounts of cyanide. It should also be emphasized that ataxic neuropathy is different from lathyrism, the disease produced by consumption of certain
Lathyros peas (see Chapter 7, p. 155). While the toxic compounds in these legumes are nitriles (i.e., they contain the -CN functional group), they do not give rise in metabolism to HCN and therefore are not cyanogenetic.

As attention focuses on the possibility of chronic cyanide toxicity from dietary sources of HCN, notice should be paid to other sources of HCN as well as to possible therapeutic measures. The blindness occurring in some heavy smokers (tobacco ambyopia) may be due to poisoning by the HCN that is a component of cigarette smoke.1-3 This condition in man, and other neurological conditions induced in animals receiving dietary cyanide, has been treated therapeutically with the hydroxocobalamin form of Vitamin B12, which has a high affinity for cyanide.4 Earlier mention has been made of the fact that thiocyanate formed by detoxification of HCN is itself a goitrogenic agent (p. 303). It is not surprising, therefore, that a widespread incidence of goiter has been reported in eastern Nigeria5 where a dry, unfermented form of cassava is a major item of the diet.

In view of the problems associated with the consumption of cyanophoric plants by man and other animals, it is interesting to note the biosynthetic origin of the cyanogenic glycosides.6 Most of the glycosides listed in Table 1 are formed from four naturally occurring amino acids: valine, isoleucine, phenylalanine, and tyrosine. A biosynthetic pathway leading from these amino acids to the aglycones of the glycosides has been proposed, and supporting evidence has been cited.7 In recent work, enzymes catalyzing certain of the reactions in the pathway have been partially purified from linen flax and sorghum and their properties examined. Of considerable biochemical interest are two facts: the -CN or nitrile moiety of the aglycones is derived from the carbon and nitrogen atoms of the parent amino acid; and the intermediates involved are compounds not previously encountered in the metabolism of amino acids in animals and microorganisms.

REFERENCES

"THE MOST HEARTLESS"

"Of all the ghouls who feed on the bodies of the dead and the dying, the cancer quacks are most vicious and most heartless."

—Morris Fishbein, 1961

"Suppose you suddenly discovered that you have cancer. A horrible, crab-like disease has invaded your body, gnawing your flesh, has pushed greedy tentacles into your vital organs. A fleshy scavenger slowly and inexorably is consuming you, cell by cell."

With these stark words one of the 20th century's most successful cancer-treating irregulars opened his autobiography, catching eagerly the lurid and repulsive image in which mankind has conceived of cancer through the ages. The word "cancer" derives from the Greek word for "crab." The crawling spread of cancer, whether external and observable or internal and secretive, is relentless, and during long centuries the diagnosis of cancer has amounted to a sentence of death, following a painful and often protracted decline.

During the 20th century, important headway has been made in combating this ancient disease. The basic processes involved in cancer's various forms are better understood. Diagnostic techniques are constantly improving. Great advances in therapy have come through improvements in surgery and in the use of x-rays, radium, and other radioactive substances. "The cold knife and the hot rays" really produce cures. Nearly a third of all patients with cancer are now being saved, as judged by the fact that they are still alive five years after diagnosis, and this proportion could be raised to a half with prompt and full application of the knowledge and skills possessed by our specialists.

But the age-old fear of cancer still persists. Indeed, relatively, the image of cancer has grown more grim. For the gains in fighting it have been less dramatic than medical triumphs in other areas, especially with respect to contagious diseases. Despite massive research, chemotherapy for cancer has so far yielded only modest results. Drugs can postpone death in patients afflicted with certain forms of cancer. A few antibiotics have caused some profound remission, if not cure. One rare type of cancer, treated with a combination of drugs, has yielded a high rate of five-year cures. But no chemotherapeutic agent has been found that can vanquish cancer as penicillin can often cure pneumonia. So, in the scale of killers, cancer has risen, now ranking as the number two cause of death, destined to end the lives of one in four of every eight Americans.

The fear of cancer has doubtless been aggravated by the very necessary effort to combat it. For the word itself has appeared so often in the press during the last generation that latent concern has been constantly quickened into conscious dread. Educational campaigns have aimed at leading the public to recognize symptoms and to seek diagnosis early enough for surgery or x-ray treatment to be effective. This effort has brought continued life to many who would have otherwise been doomed. Yet as inevitable side effect of increasing cancer-consciousness has been a rise in cancer quackery. For fear of cancer, fear that some ambiguous symptom may mean cancer, fear of surgery and radiation if one has or might have cancer, fear of the waiting period after orthodox treatment to determine its success or failure, fear that discovery has come too late to warrant treatment, fear, agonizing numbing fear, overwhelming the safeguards of rational prudence, sends desperate men to the cancer quack.

Not that the cancer quack is a new breed, of course; he has been around almost as long as the malady itself. He flourished in the 19th century, offering his "secret specific" to the frightful..."
end, who, "like a drowning person grasping at straws, seized upon the frail hope that is offered by the hand of ignorant charity." Within the 20th century, all foes of the charlatan have been forced to keep him constantly in mind. The Sherman Amendment was provoked by the Bureau of Chemistry's loss of a cancer labeling case. Post Office fraud fighters have won a succession of victories over mail-order "specialists" in treating cancer. But Dr. Cramp, in successive editions of Nostrums and Quackery, noticed no diminution in their sordid ranks. Hardly a week passed without the receipt in his office of a letter announcing the discovery of a "sure cure" for cancer. Nor did pseudo-science waver during the decades that science was making its most notable advances. By the 1930's, some 4,000 quacks were fleecing thousands of victims who had or feared they had cancer out of about $50 million every year.

In 1936, the year in which Dr. Cramp published the last green-bound volume in his Nostrums and Quackery series, one of the key characters in Cramp's cancer cast showed up in Dallas, Texas. There, in a small one-story building, Harry M. Hoxsey opened a cancer "clinic." This venture, unlike a number of Hoxsey's previous efforts which Cramp had chronicled, turned out to be a major financial success.

Hoxsey had inherited the cancer business. Early in his career he gave his father credit for the discovery of his remedy, setting the date at 1918. Later on Hoxsey told a more grandiloquent tale, pushing the date back to 1810 and transferring the distinction to his great-grandfather, who, on his Illinois farm, observed how his Percheron stallion cured a cancer of the right hind by standing knee-deep in a clump of shrubs and flowering plants. In both accounts, Hoxsey's father, a self-taught veterinarian, employed the secret anti-cancer remedy first on livestock, then on men. The elder Hoxsey died in 1910, and the cause of death was cancer, a fact his son later went to great pains to deny. Harry's mother died two years later, also

**THE MOST HEARTLESS**

of cancer. In 1921 Harry was 20, and life did not look promising. The youngest of 12 children, Harry had grown up in the rural Illinois village of Girard, had quit school after the eighth grade—he later claimed receipt of a high school diploma from a correspondence school—and had gone to work in the coal mines at neighboring Taylorville, selling some insurance on the side."

Young Hoxsey was an ambitious fellow, "quick-brained" and "ingenious," as a federal judge later remarked, natty in dress, glib and persuasive of speech. As one of his early admirers put it, "Harry is not a man of few words but one of many," and those words, not elegant in grammatical construction, definitely possessed the common touch. His endeavors were early imbued with the spirit of the motto he later displayed on a desk plaque: "The world is made up of two kinds of people—dem that laces and dem that gets took."

Some of his siblings were shortly to sue Hoxsey, accusing him of taking their father's cancer formula for his own profit, after his mother's death, a legacy that should have belonged to them all. The suit was never pushed to a conclusive decision. Harry's story had it that his father, just before his death, had taught him the formula by having him copy it 250 times until he learned it by heart and had given him a dramatic death-bed injunction to devote his career to healing the sick, no matter what opposition he might encounter from "the High Priests of Medicine." In any case, Harry claimed, he had changed the composition of the formula."

*The Hoxsey Method of Successfully Removing Cancer (Taylorville, 1928), in Hoxsey folder, AMA Dept. of Investigation; Hoxsey, You Don't Have to Die, 67-76. The AMA Hoxsey folder contains much data on the cause of Hoxsey's father's death, and the FDA discovered that Hoxsey wrote the Illinois State Registrar for a copy of his father's death certificate using an incorrect middle initial, receiving a reply that no certificate could be found. The initial was corrected in the copy of the Registrar's letter by reptitit in You Don't Have to Die. Interview with Gilbert Goldhammer, Nov. 17, 1960.*

"Judge William H. Atwell's oral opinion, Mar. 18, 1949, in Harry M. Hoxsey v. Morris Poblete et al., in the U.S. District Court for the Northern District of Texas, Dallas Division, copy in FDA file, Injunction 252; Girard (Ill.) Casino, July 18, 1929; Life, 40 (Apr. 10, 1938), 125.
*AMA Hoxsey file; Hoxsey, You Don't Have to Die, 71-74, 141-53.*
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About 1922 Hoxsey began to use the formula. As he later told the tale, a Civil War veteran with cancer of the lip had come to him and begged for treatment. Harry had demurred, saying he had no license to practice medicine. "Nobody needs a license to save lives," the veteran had argued. "If I was drowning would you stand by and watch me go down because a sign on yonder tree says 'No Swimming Allowed?'"

"There's no adequate answer to that kind of logic," Hoxsey said in retrospect, "and I didn't waste any time trying to find one."

He used the cancer paste on the venerable veteran, who thereafter, throughout his life, was willing to testify in public utterance and in print that he had been cured.

While practicing sporadically in Taylorville, Hoxsey joined up with two Chicago men to form the National Cancer Research Institute, a common law trust to exploit the use of his father's formula. When his associates backed out of this enterprise to give their support to another cancer venture, Hoxsey expanded his Taylorville operations into the Hoxside Institute. Supported by some of the town's businessmen, Hoxsey took over from the Order of the Moose an old frame house and began to advertise his treatment far and wide. "Cancer," the copy read, "Any person suffering from this malady . . . is invited to apply for authoritative information as to the cures that have been effected and are now being effected at Taylorville, under strictly ethical medical supervision, painlessly, without operation, and with permanent results." Inquirers were told to write the secretary of the Taylorville Chamber of Commerce.

Patients responded to the advertising, and shortly the local paper began to run stories of deaths that were occurring at the Institute. Local doctors began to be concerned. One of them wrote the "high priests" at the American Medical Association telling of examining a man who had received the Hoxside treatment. The paste had been applied to a tumor on the cheek. "Two days before . . . [the man] died," the doctor wrote, "I was called to see him and found necrosis of not only the soft tissue of his face, but a complete destruction of the malar bone. This man died of hemorrhage at the hospital."

To keep the secret of his medicine, the doctor said, Hoxsey bought the separate ingredients each at a different drugstore. The key ingredient, analysis at AMA headquarters revealed, was arsenic. Thus Hoxsey's vaunted remedy was an escharotic, a corrosive chemical that ate away the flesh. Through the ages physicians had employed such corrosive agents in treating external cancers, but this mode of procedure had become outdated. "Pastes went out with the bustle," a cancer authority has noted, "so far as scientific medicine is concerned." Such chemicals could not distinguish between tissues that were cancerous and tissues that were sound. The risk of damage to healthy flesh was tremendous. The escharotic might eat into the blood vessels and cause death through bleeding. Surgery was much safer and more certain.

The goings-on at Taylorville brought Hoxsey into conflict both with the AMA and with the law. Dr. Cramp blasted the Hoxside Institute's methods in the AMA Journal. Tragedy awaited "sufferers from carcinoma," he wrote, "who are beguiled by false beacons displayed by the highly respectable citizens of Taylorville" into resorting to Hoxsey's treatment. He detailed instances of tragedy that already had occurred. "The promoters of the scheme" were reaping "a rich harvest from gullibility and suffering."

Hoxsey sued the AMA in response to its criticism, asking a quarter of a million dollars in libel judgment. The case dragged on, and finally the AMA insisted that it be brought to trial. The Hoxside Institute was not prepared, and the judge dismissed the suit. In the meantime, Hoxsey had gone to court as defendant instead of plaintiff. Charged with responsibility

11 Ibid., 76-77.
12 AMA Hoxsey file; JAMA, 86 (Jan. 2, 1920), 55-57.
for the death of one of his victims, he was accused of practicing medicine without a license. He pleaded guilty and paid a $100 fine.

The Hoosick Institute in Taylorville closed its doors in 1928, but Harry Hoxyse did not abandon the corrosive legacy inherited from his father. Twice again in quick succession he sought to duplicate his Taylorville venture in Illinois towns, first in Jacksonville, then in Girard. He launched his return to his home town with a Sunday “Hoxyse Day,” under the aegis of the Chamber of Commerce, a day that had all the trappings of a Fourth of July celebration. The Girard band played, lying testimonials from among the citizenry, including the Civil War veteran, bespoke their gratitude to Hoxyse before the large audience assembled in the town square under a boiling sun. A celestial doctor from Indiana hailed the Hoxyse method. A local minister delivered an oration imbued with religious and patriotic zeal. “I love my country,” he told the crowd, “because its heroes are such characters as George Washington, Abraham Lincoln, Woodrow Wilson, who love to serve and not to rule. I love Hoxyse because he does not want to rule the world but serve the world.”

Hoxyse himself addressed his former neighbors. “There is a lot of knockers,” he said, “who do not know what they are talking about, and especially around a man’s home town, and if these knockers are here today and have the mind of a six-year-old child and don’t leave here today, a walking, talking dyed-in-the-wool Hoxyse fan and convinced beyond a reasonable doubt that this treatment is a cure for cancer they are either deaf, dumb or blind, or else they are crazy.” Regular doctors were “hard-hearted,” interested in getting “their hands greased with plenty of money,” wanting to drive their Packards and their Studebakers. AMA officials had been invited to attend the rally, but they had not come. “Why don’t they fight in the open? Why don’t they take this platform? Why don’t they prove the Hoxyse affair is a fake as they say? . . . But no, friends, they haven’t got the guts to accept this challenge.”

And Hoxyse presented his gallery of patients who said they

14 Ibid., 83 (Aug. 3, 1929), 400-402.
15 Ibid., Girard Gazette, July 15, 1929.

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had been cured, quizzes them publicly on the details of their experience. “Anyone in the hearing of my voice,” he challenged, “who will prove that the Hoxyse Method does not cure more than 50 per cent of its patients, or if they will prove or show that there is another method under God’s skies as good as the Hoxyse, he can receive the reward which we have offered on our large posters.”

Applause was frequent, the local editor observed, and when one speaker asked if the audience wished to endorse Hoxyse in his attempts to save lives, “the response was so nearly unanimous that those who remained sitting for any reason could be counted on the fingers.”

If the citizens were impressed, the AMA was not. "Perhaps," Cramp wrote, "Girard will flourish briefly—especially the local undertaker and those individuals who have rooms to rent. . . . If that is what the citizen—. . . want, the Hoxyse fakery will doubtless grow to them. They will also get the dreadful privilege of the reputation of living in a town that fattens on the sufferings of those unfortunate who are bled there by the false hope that an ignorant faker has discovered a 'cure' for one of the most-dreadful scourges afflicting the human race.”

Hoxyse's Girard endeavors were indeed brief, and twice more he paid a fine for practicing in Illinois without a license. A cooperative venture across the river in Iowa did not work out much better. Hoxyse teamed up in Marseville with another uneducated promoter of a cancer cure, Norman Baker, but the two fell out, the state stepped in, and Hoxyse was barred by injunction from treating cancer patients. During the next several years, Hoxyse was much on the move. He set up shop in Detroit, in Wheeling, then in Atlantic City. Wherever he went, the AMA dogged his footsteps. Legal actions were sometimes instituted. Finally, in 1936, Hoxyse went south. Dallas promised to be a safer and more prosperous haven, at least for a time.

As had been true beginning with his Illinois enterprises, Hoxyse strove to concentrate on the business and promotional sides of his Dallas clinic, leaving the diagnosing and treating
mainly to a series of eclectic, homeopathic, and osteopathic physicians whom he employed. But he could not bring himself to abandon completely from therapy. Again convicted of practicing medicine without a license, Hoxsey was fined $25,000 and sentenced to five months in jail. A higher court, however, set aside this verdict. Hoxsey managed to acquire an honorary Doctor of Naturopathy degree and was licensed in Texas as a naturopath.

Hoxsey's early years at Dallas coincided with the early years of the chemotherapeutic revolution. His burgeoning business owed not a little of its success to this fact. For, in addition to treating external cancers with escharotic substances, the clinic offered to treat internal cancers by "chemical" means. Hoxsey was to claim that his internal medicines had been used by his father and inherited from him. But the evidence seems to suggest that, in his Illinois days, only the corrosive paste was employed in therapy, used to be sure, not only in treating skin cancers, but also for cancer—or purported cancer—of the breast and female organs. Exactly when he began using his "tonics" for hidden cancers within the body is not clear. Perhaps he acquired his formulas from Norman Baker during the temporary joint operation in Mexico. At any rate, in his early Dallas days, Hoxsey boasted he could cure internal cancers with medicines. To a public increasingly fearful of cancer and increasingly hopeful of chemotherapy, such an appeal offered a glimmer of hope.

The ingredients in Hoxsey's internal medicines, kept secret until revealed in court actions, varied somewhat from time to time. Two liquid mixtures played the central role, one brownish-black in color, the other pink. The brownish-black liquid contained water, potassium iodide (used mainly in medical practice as an expectorant to loosen tenacious sputum in cases of bronchitis), cascara sagrada (an herbal laxative), sugar syrup, and usually prickly ash, buckthorn, alfalfa, and red clover blossoms. The pink liquid, besides the other ingredients, contained lactate of pepsin, a vehicle used to help the stomach tolerate nauseating medicines; the pink variety was prescribed when patients encountered some of the unpleasant side

effects occasionally experienced when taking potassium iodide.

Why his colored mixtures cured cancer, Hoxsey and his spokesmen were frank to confess they did not completely know. "We have been too busy treating cancer victims—and fighting court battles to keep our clinic open—" he asserted in his autobiography, "to spare the time, personnel and facilities for objective study." His hypothesis, in its limited version, held that a major chemical imbalance in the body caused normal cells to mutate into a cancerous form, and his medicines restored the original chemical environment, checking and killing the cancerous cells. This hypothesis could be elaborated at length—as in an address delivered by Hoxsey's medical director—into a complicated fantasy of irrelevant scientific and pseudo-scientific jargon that sounded very impressive to the layman but caused genuine cancer experts to groan. What made things worse, as the experts assessed the Hoxsey theories, was that the Hoxsey literature condemned the only treatments yet found valid in cancer therapy. "In my opinion," wrote medical director J. B. Durkee, "x-ray and radium have no place in the treatment of cancer... They further upset basic cell metabolism rather than do anything to correct it." Durkee's lecture, in printed form, played a prominent role in Hoxsey's "scientific" confrontation of his would-be patients.

Equally important in that confrontation were testimonials from other patients just as on "Hoxsey Day" at Girard, so in Dallas Hoxsey could present "satisfied" users of his methods, men and women who credited him with saving their lives. They would respond to letters from inquirers, talk to investigating groups, testify in court, and write their touching expressions of gratitude for Hoxsey to print and distribute far and wide.

Hoxsey's promotional documents did not claim that all can-

28 FDA file, Inj. 232, JAMA, 155 (June 12, 1951), 667-68; Transcript of Record in the United States Court of Appeals, Fifth District, No. 136, United States of America, Appellant, versus Hoxsey Cancer Clinic, a Partnership and Harry M. Hoxsey, an Individual, Appellee (Fort Worth, 1931), 60-84.

29 Hoxsey, You Don't Have to Die, 41-46; Durkee address in Hoxsey Cancer Clinic, Specializing in Cancer, in FDA file, Inj. 232.

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cancers could be cured. Indeed, he specifically denied this was the case. Cures were less certain if x-ray or radiation treatment had been used first. But with Hoxsey's "entirely revolutionary" internal medicine, many cancers could be cured. The cure rate for breast cancer, for example, according to Dr. Durke's speech, was 50 to 60 per cent. And counting his cures, in the minds of those who read Hoxsey's literature, were the compelling case histories.

When a fearful patient showed up at the door of Hoxsey's first small-Dallas clinic, or later at the larger building which growing business had led him to acquire, the patient's case history was transcribed by a clerk. The sufferer's own suspicions were taken down, plus a record of anything he had been told by doctors whom he might have consulted earlier. Discouraging records of previous diagnosis or treatment like the results of a biopsy, were solicited. Then came some laboratory tests: various blood studies, a urinalysis, a test for syphilis. Very rarely a biopsy was secured. Chest and pelvic x-rays were made and a general physical examination given by a member of the staff.

The medical director reviewed the records and, if cancer was diagnosed, prescribed the Hoxsey treatment. Patients said to have internal cancer were treated with Hoxsey's current version of the escharotic powder. They and patients said to be suffering from internal cancer were put on the internal medication, usually the brownish-black liquid first, then two teaspoons a day. "Supportive" treatment of vitamins, inactives, and antibiotics was also prescribed. Then the patient saw the business manager and arranged for the payment of the patient's charges: the basic fee in Dallas was first $300, later increased to $500, plus certain other costs. Hoxsey insisted, as he had asserted throughout his career, that many indica patients were treated free.

As the years went by, thousands of patients from all over the nation made the trip to Dallas, learning of Hoxsey through his printed pamphlets or by word of mouth. Some had diagnosed their own symptoms without consulting doctors and had reached the fearful decision that cancer had attacked them. Others, with cancer diagnosed by physicians, sought out Hoxsey instead of submitting themselves to surgery. Still others had already undergone operations and x-ray treatments, but in their despair determined to miss no bets. The Dallas methods were also exported to other states. A few physicians and osteopaths around the country, after spending some time in Dallas, returned to their own cities and sought to treat cancer the Hoxsey way, receiving by mail their supply of the brownish-black and pink tones.
unwilling or unable to provide the type of sophisticated data from which expert scientists could draw valid conclusions. When scientists rejected proffered tests, on grounds that the data were insufficient, it was easy for the promoter to raise the ancient cry of perdition. Physicians did not dare find out the truth, he could say, for fear that their lucrative methods of treatment might become outdated. This pitch too brought sympathetic response from many laymen, well aware that regular medical treatment often was expensive. Such an appeal played also on a latent suspicion of complicated science that was present, as well as awe and respect, in the mass mind.

Hoxsey continually proclaimed that he wanted tests. In the year that Senator Thomas visited him, Hoxsey wrote the Texas State Medical Board: "If you will come out here to the clinic and we cannot prove to you that we have cured cancer after radium, x-ray, and surgery had failed, we will give you $10,000, or better still, we will take 25 cases of cancer and let the entire Dallas County Medical Society or any doctor in America take 25 cases, and if we do not cure two to their one in sixteen weeks, we will donate $10,000 to any charitable organization in Dallas County." Two years later Hoxsey expressed his eagerness for testing to two scientists who visited the clinic. The next year he again submitted case data to the National Cancer Institute and again, after careful appraisal, the Institute determined that the material did not meet its basic requirements. Hoxsey's 77 case reports were accompanied by only six biopsies; only two of these were from patients treated for internal cancer, neither of which revealed anything that could be identified as cancer cells. Despite this, a committee of the National Advisory Cancer Council perused the Hoxsey records case by case. No single case met the Council's criteria. Clinical tests were naturally refused.\footnote{AMA Hoxsey file; reports to the American Cancer Society on a visit to the Hoxsey clinic, Feb. 10, 1940, by L. T. Coggsall and Andrew C. Ivy, attached to "Hoxsey 'Cure for Cancer," Committee on Cancer Diagnosis and Treatment, L. R. Heller, Director, NCI, to Sen. William Langer [May 1951], copy in FDA file, Inj. 232.}

By this time Hoxsey had interested another Senator in his operations. William Langer of North Dakota had already gone...
men," and patients had the right to go to them for treatment. "Pay your money," Judge Atwell said, "and take your choice." The judge seemed to have been much impressed by the testimony of the satisfied users whom Hossey had paraded to the witness stand. They said they had had cancer, and they said they had been cured. "Healing," Atwell was persuaded, had occurred, and the circumstances brought to his mind the healing of Christ.

Judge Atwell was asked on the bench, in 1930, the government sought to enjoin Hossey from shipping his medicines for internal cancer across state lines. Not until this date had court decisions broadened the definition of labeling under the 1922 law so as to make it seem applicable to Hossey's methods of operation. The Food and Drug Administration first instituted a seizure action against tonics sent from Dallas to a Hossey practitioner in Denver, but Hossey let this action go by default. Now, in Judge Atwell's courtroom, he fought.

Food and Drug officials had worked prodigiously to develop a persuasive case. Their goal was to demonstrate the ineffectiveness of Hossey's tonics in treating internal cancer and to disprove Hossey's oft-repeated claims that cases had been cured. Dr. David L. Macht, a distinguished specialist in pharmacological and experimental therapeutics, long a Johns Hopkins professor, was called to the stand.

"Doctor," he was asked by the district attorney, "is there any recognized therapeutic use of any of these items [in the tonics],"

31 Judge Atwell's oral opinion, Hossey v. Fishbein.
32 FDA file, Inj. 232; DIONI 3288.
33 FDA file, Inj. 232; Transcript of Record, passim.

The AMA had not forgotten Hossey, and in 1917 Fishbein had written an excoriating editorial in the Journal entitled "Hossey—Cancer Charlatan." To warn a wider audience, Fishbein also co-authored an article called "Blood Money" for the Hearst chain's weekly magazine section, carried by the San Antonio Light. Fishbein repeated the phrase "cancer charlatan" in reference to Hossey and termed his father "a veterinarian and dabbler in faith cures" who had himself succumbed to cancer after claiming to have found a cure for it. Hossey promptly sued, asking a million dollars libel damages.

He won the case, receiving, however, not a million dollars but only two, one for himself, one for his father. Elderly Judge William Atwell, who heard the case, concluded from the testimony that Hossey had made no claim to be a physician but only a charlatan. Atwood's oral opinion, May 28, 1917, copy in FDA file, 232; Sen. Rec. 112, Cong. Rec. 82 Cong., 1 sess., 1951.

Although Hossey's patients failed to recognize the therapeutic value of his tonics, he had still managed to build a sizable fortune from them.
and other items, any therapy for malignant cells, that you are aware of?"

"Absolutely no basis for it," he replied, "and I am speaking not only as a pharmacist, but as a member of the American College of Physicians."

Potassium iodide, indeed, another specialist testified on the basis of his own researches, "would speed up the growth of cancer." Horsey's tonics, still another noted cancer research scientist said, had not cured cancer in mice. In an experiment which he conducted for the Food and Drug Administration, malignant growths in mice treated with the medicine were uniformly larger at autopsy than at the beginning of the tests.

In preparing for the trial, Food and Drug inspectors had tracked down the case histories of scores of Horsey's patients. Men, women, and children who had talked with Senator Thomas, those whose names were used in Horsey's promotions, those whose cases had been submitted to the National Cancer Institute, all were investigated. Patients still living were talked with; members of the families of those who had died were interviewed. Physicians with whose cases Horsey's patients had consulted before or after going to the Dallas clinic were queried, their records checked. Hospital records, the records of pathological clinics, were studied. Horsey's former employees were questioned. From all this inquiry a pattern emerged. This pattern the government sought to make clear in court. Selecting 16 cases—nine of them persons whose testimony had been given in Horsey's pamphlet considered as labeling—the government called to the stand the patients or their survivors, diagnosticians, pathologists, surgeons, and other scientific experts. Horsey's claimed "cures" of internal cancer as represented by these typical cases, the government sought to show, all fell into three classes. Either the patients had never had cancer, although treated for it at the Dallas clinic. Or they had been cured of cancer by proper surgical or radiation treatment before consulting Horsey. Or they had had cancer and either still were so afflicted or had died.

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school boy of 16 who, after a football injury, developed an extremely malignant cancer in a leg bone. When the boy's physician recommended amputation, the parents could not face this prospect and took their son instead to Horsey's clinic. The medical director, the father testified, had guaranteed a cure. For some four months the lad took Horsey's tonics. They did no good. Several months later the boy was dead. Had the amputation been performed, the physician who had first treated the boy testified, he would have had a fighting chance.47

Horsey, who did not take the stand himself, based his defense mainly on another round of testimonials. Indeed, some of his former patients who were government witnesses continued, despite the evidence, to express their loyalty to him. Twenty-two other patients took the stand for the defense to lay Horsey's treatment. Half of these cases had been treated for skin cancers with Horsey's escharotic powders and pastes. The issue of the external treatment was not on trial, but Judge Atwood let these witnesses testify anyhow. Cancer specialists did not deny Horsey might cure some cases of skin cancer with his tissue-eating chemicals. The method, however, was outdated and unnecessarily painful and hazardous. Modern surgical and radiation techniques could cure upwards of 95 per cent of such cases more safely and humanely.48

Of Horsey's 11 patients testifying that they had been cured of internal cancer, the only evidence that three had ever had the disease was their own affirmation. In four other cases, the government introduced rebuttal testimony to show that the patients had been cured before consulting Horsey. In the four remaining cases, the sole evidence that the patients had indeed had cancer was the testimony of Dr. Durkee, Horsey's medical director. In cross-examining Durkee, the district attorney brought out the inadequacy of his qualifications to speak with authority in this field. A 1911 graduate of a Chicago osteopathic college, Durkee had interned for less than a year at a small unaccredited osteopathic hospital in Nebraska, where he had seen only four or five cases of cancer. Then he had practiced for several years in a Texas village, encountering perhaps

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10 to 15 cancer patients. In 1916 he had joined Hossey's staff. There he had seen some 35 to 50 patients a day, examining each one for an average of five to ten minutes. He did not "need a biopsy to make a diagnosis of cancer," he testified, and rarely used the technique. Biopsies that Durkee had submitted to pathological laboratories, other evidence showed, were so poorly prepared as to be useless. His knowledge of the pharmacological action of the drugs in the Hossey tonics was vague, his explanation of the Hossey theory of cancer and its cure as false from the witness stand as in his public address reproduced in the labeling pamphlet.

Despite Durkee's confession, despite the government's carefully presented case, Harry Hossey won in the contest. Judge Atwell would not grant the injunction. He could not agree that Hossey's treatment was either injurious or futile. "Some it cures," he ruled, "and some it does not cure, and some it benefits somewhat." Its "percentage of efficient and beneficial treatments," the judge decided, was "reasonably comparable to the efficiency and success of surgery and radium."

Atwell's decision did not surprise FDA officials. His admission into the record of the self-diagnosis of cancer by Hossey's lay witnesses, his willingness to hear testimony about external cancer, had been straw in the wind. In any case, the Food and Drug men suspected that Atwell himself had once been a Hossey patient.

The government appealed. Persuaded that Atwell had been swayed by incompetent testimony, that he had misapprehended the impact of evidence presented by medical experts, the government asked the circuit court to grant the injunction which Atwell had refused. After a careful scrutiny of the two large volumes of testimony, the three-judge court unanimously acceded to this request. A layman's opinion as to whether he had had cancer and been cured, the judges said, was "entitled to little, if any, weight." Only a biopsy could permit accurate diagnosis. Only surgery, x-ray, and other radioactive substances could cure; such was the judgment of the "overwhelming weight of disinterested testimony." A judge "should not be so blind and deaf as to fail to see, hear and understand the import and effect of such matters of general public knowledge and acceptance." Hossey's entire promotional campaign sought to persuade the cancer sufferer that "he had an excellent chance to be one of those cases in which the medicine would be successful." Yet with respect to Hossey's own testifiers in his labeling, the government had demonstrated that the brownish-black and pink tonics had not proved efficacious. Atwell had erred, therefore, abusing his discretion. He must grant the injunction which the government had sought.

Before Atwell could ponder this directive, Hossey asked the Supreme Court to reverse the circuit court's decision. But the highest tribunal would not grant certiorari. So Atwell yielded to the circuit court's demands. The injunction he issued, however, followed a form suggested to him by Hossey's attorneys rather than the form presented by the government. The decree did not bar Hossey's internal medicines from interstate commerce. It forbade their interstate shipment unless—and here was an effort to appeal to the McAnulty decision of half a century before—"unless they were labeled to show that there existed a conflict of medical opinion concerning their curative claims. Such a ruling, Food and Drug officials knew, would shut no doors at all."

Since the circuit court had found as fact that Hossey's internal remedies could not cure cancer, no legal room existed for the assertion of differences of medical opinion. So the government sought from the circuit court a writ of mandamus that would require Atwell to issue the injunction in the proper form. In the legal maneuvering over the writ, Hossey again appealed to the Supreme Court and was denied. The circuit court, using a less rigorous remedy than a writ of mandamus, nonetheless made it clear to Atwell that the disputed clause in his injunction was in "direct conflict with the court's earlier...
"THE MOST HEARTLESS"

One of Hoxsey’s new allies in his expanded fight was Gerald B. Winrod, the Kansas evangelist. A militant fundamentalist, Winrod had fought modernism in religion during the 1920’s. Later, he turned his attention to right-wing politics, providing the inspiration for Sinclair Lewis’ portrait of “Buzz” Windrip in It Can’t Happen Here. A visit to Germany in 1934 confirmed Winrod’s pro-Nazi inclinations, although he played this down while neatly winning the Republican Senatorial nomination from Kansas in 1938. During the war he was indicted for sedition for expressing views calculated to impair morale in the armed forces, but the death of the judge halted the trial. After the war, Winrod’s personal organ, the Defender, brought a hundred thousand subscribers a mixture of fervent fundamentalism in religion and morals, right-wing political extremism, violent ‘antagonism’ toward Jews and Negroes, hostility to modern medicine and mental health programs. The Defender also accepted flying saucers and championed unorthodox healers.

Winrod helped publicize Glyoxylide, the cancer remedy devised by a Detroit physician, William Frederick Koch. A group of ministers in Winrod’s circle even set up a religious front, the Christian Medical Research League, to market this purported cure. And Winrod also joined hands with Hoxsey. Over many months the Wichita evangelist praised the Dallas clinic in the pages of the Defender, in pamphlets, in a book, in radio speeches. Winrod’s motives were not unmixed. Although he asserted that he himself, when young, had been cured by the Hoxsey treatment—a tribute which Senator Langer inserted in the Congressional Record—Winrod’s publicity, whatever his gratitude, was not freely given. According to evidence later introduced in court, Hoxsey paid Winrod over $50,000. This fact was not apparent to Defender readers who learned of Hoxsey’s marvelous “cures” along with their fundamentalist Sunday School lessons. After a Hoxsey defeat in court, Winrod wrote a letter to his constituency asking them to offer “daily, persistent, argumentative prayer” for Hoxsey, according to Luke 18:17. Winrod asked...
more funds to carry forward Hossey's "anti-cancer crusade," and the names and addresses of at least five cancer victims to whom Hossey's literature might be sent, Winrod signed this appeal "Yours in Christ's Service." 24

Hossey had other similar allies. The American Rally was an isolationist organization, established in 1952 "For Peace, Abundance and the Constitution." Like Winrod's journal, it opposed fluoridation and polio vaccine and believed in flying saucers. In 1955 the Rally's magazine came out for Senator Langer for president in the 1956 election, landing him at the "Alphonso Lincoln of the 20th Century." Shortly the Rally discovered a vice-presidential candidate fit to run with Langer; his name was Hossey. Introducing Hossey to a Rally convention in Chicago, its executive head said, "The spirit of Lincoln is here tonight." Hossey responded with such Lincolnian phrases: "The Yankee killed my daddy. . . .the same bunch of rats I've been kicking ever since." 25

The American Rally shared with other dissident groups belief in "medical freedom," defined as the right of every individual to seek treatment from Hossey's clinic and other clinics and practitioners, owned by the orthodox medical profession. Two such groups were the American Association for Medico-Physical Research and the American Naturopathic Association. Hossey and his associates spoke before their meetings. At a naturopathic convention in Chicago, Hossey addressed himself to the theme, "Who Are the Real Cancer Quacks and May God Have Mercy on Their Souls." From the same room during this meeting, an address was also given by Fred J. Hart. 26

Hart was one of Albert Abrams' many heirs. Listing his fields of endeavor as "Agriculture and Research," Hart had been associated with the College of Electronic Medicine, which sought to keep Abrams' doctrines flourishing, as early as 1915 and had become president by 1916 when the name was changed to the Electronic Medical Foundation. In 1954 the government had secured an injunction banning shipment in interstate commerce of numerous therapeutic machines fabricated by the Foundation. Hart was the moving spirit, the next year, in creating a new group to fight for "medical freedom," the National Health Federation. Hart became president, one of Hossey's lawyers served as legal representative in Washington, and several of the FDA's most stubborn antagonists sat on the Federation's board. At membership rallies in California, Hart pleaded for funds to help Hossey carry on his fight, and Hossey asserted that he was giving the royalties from his autobiography to help finance the Federation. 27

The Food and Drug Administration was not an independent agent, spokesmen for the Federation charged. As Hart once put it, Commissioner "Larrick has to do what the medical trust tells him or he'll lose his job and he wouldn't like to wash dishes for a living." The medical profession, the drug industry, the food manufacturers (who added "poisons" to their cans), according to the Federation's journal, were all allied against the people. "The House of Rockefeller" owned "the drug, food, milk, serum, news and money trusts" and it owned the Eisenhower administration too. As a result, the FDA's administrative actions were marked by "vilelessness," and the agency allowed its employees "to blackmail and slander firms and individuals without restraint." The Federation aimed at making the FDA "a servant of the people; rather than hearing it as it now is—a ruthless enemy, at blanco [sic] in its actions as any

25 American Rally membership card; printed flyer announcing 1953 convention, American Rally, Feb., Mar., and Oct. 1953; announcement of Apr. 1955 Chicago meeting; memorandum on Hossey address at Chicago convention, Apr. 26 1955. These documents are in FDA file, Interstate Science No. 4-054.
26 Program for Aug. 1959 convention in Chicago of the American "THE MOST HEARTLESS"

THE MOST HEARTLESS"
The cover of the Federation's magazine in which this statement appeared again appeared to Lincoln, carrying his picture—and Washington's too—and the caption, "They Too Fought for Liberty Against Great Odds."

Federation representatives lobbied on the federal and state levels, seeking an investigation of FDA policies and procedures, striving for the right of other practitioners besides M.D.'s to have access to federal research funds, seeking to limit fraud and cancer quackery control measures, trying to secure a ban on publicity by regulatory agencies about court cases until the final judgment was rendered, and much else. The Federation's literature flourished in quantity, seeking to win support from such groups as the Gold Star Mothers and the DAR. Petitions to Congress were sponsored, many in behalf of Hoxsey, asking an investigation of the FDA. Nearly 200,000 petitions had already reached the Capitol, Hoxsey told a Federation meeting in California in 1957, and this was "driving" the FDA "nuts." Letter-writing campaigns were also stimulated among the faithful. "Using specialists in mass psychology," Commissioner Larrick stated, "the promoters held numerous meetings under the guise of 'scientific lectures' to organize a protest movement among these prejudiced against recognized medical treatment. They used radio, television, circulars, religious publications and even large barnside signs, to encourage the public to write to Congressmen and the President, demanding investigations of FDA persecution of their leaders." The faithful disciples of Hoxsey and his allies responded eagerly. "We have had," said Larrick, "a torrent of belligerent letters to answer." One result of this deliberate effort to arouse the hostility of common citizens is revealed in a sentence from one woman's letter: "I do not trust the government anymore."

Hoxsey's cancer treatment metastasized from Texas into other states, particularly Pennsylvania. There its chief champions and promoter was state senator John Haluska. Having lost his mother and a young son from cancer, Haluska gave Hoxsey credit for saving his sister's life after regular doctors had given her up. (Her physicians later testified she had been cured by x-ray before going to Dallas.) Administrator of a hospital in Spangler, Haluska had been ousted for trying to convert the nurses home into a cancer clinic according to the Hoxsey pattern. Then Haluska remodeled an appliance store and garage in Portage, a coal-mining town in the mountains of western Pennsylvania, employed one of Hoxsey's former medical directors, and offered to treat cancer sufferers. The medication was slightly different, not tonics but pills—first red and black pills, then red, green, and yellow pills, the size of small linza beans. The pills contained, however, most of the ingredients in Hoxsey's tonics. When Hoxsey visited Portage, he was welcomed with a motorcade and a banquet at which Haluska apostrophized him as "the greatest man in the country today—greater than President Roosevelt was, and greater than President Truman and President Eisenhower." Similar praises resounded through the chamber of the Pennsylvania senate, with Hoxsey taking a bow from the balcony, as Haluska in a long oration announced the opening of the Portage clinic and lauded the Hoxsey methods. To his fellow senators, Haluska also introduced Kathy Allison, a young girl from Indiana. "Here, Mr. President," he said, taking Kathy into his arms, "is that little angel who, according to medical science, had to meet the angels soon. Today she is going to school, was X-rayed last week and found to be cancer-free and is playing like any other normal child." Hoxsey had treated her; God had spared her. "Senator Haluska's Great Speech" was published in Winrod's Defender, and thousands of reprints spread across the country.

The Portage clinic opened in 1955 to brisk business. One early customer, a perfectly healthy FDA inspector, received an examination lastimg a minute or two and was told he had cancer of the prostate. Quickly Food and Drug officials and a federal marshal visited the clinic and, amid a hostile throng

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The release, despite its announcement of victories, contained a sober note. "The public should know..." the text read, "that such actions will not end the menace of this..."

But Hossey's tide had turned. The Portage clinic closed shortly thereafter. At his home base the pressures mounted inexorably. Texas court actions revoked the licenses of Hossey's doctors and granted a permanent injunction to prevent his practicing medicine in Texas. Hossey then leased his clinic to another operator. Again the FDA moved in. The agency secured a supplemental consent decree of permanent injunction by which this operator promised to write all persons who had employed the Hossey treatment since 1957 that it could no longer be obtained. Since late 1960, therefore, except for a sporadic instance here and there about the country, the Hossey method of treating cancer at clinics has disappeared. Testimonials from patients claiming "cures" by the method, however, have continued to appear in the pages of health magazines, along with formulas for the Hossey medications and the addresses of herbalists who will supply the raw ingredients from which the medications may be made.

The decade of litigation against Hossey had cost the federal government perhaps a quarter of a million dollars. This

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"THE MOST HEARTLESS"

effective victory did not provide a shield against any other wares than the clinic-prescribed brownish-black and pink tinctures and the variously colored pills. While Hossey had been the largest unorthodox cancer promoter of the 1950's, he had had competitors. During the efforts to close the Portage clinic, a world-noted cancer authority, Dr. David A. Karnofsky, had addressed the American Cancer Society's Pennsylvania division. Besides Hossey's treatment, he said, 13 other major promotions were available to Americans who feared they had cancer. In 1969 the American Cancer Society, issuing a catalogue of Unproven Methods of Cancer Treatment, came up with a list twice as long as Dr. Karnofsky's.

While the scientific search went on, in public and private laboratories, for chemicals that might better aid in controlling cancer, the unscrupulous and misguided continued to tell Americans that the miraculous discovery had already occurred. Among the fearful and the desperate, these false prophets continued to find victims for their worthless wares.

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Oxidation of Thiocyanate to Cyanide Catalyzed by Hemoglobin

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SUMMARY

Thiocyanate ion is oxidized at acid pH by hydrogen peroxide to sulfate and cyanide. The reaction is catalyzed in the erythrocyte by hemoglobin acting as a peroxidase (donor: O$_2$, oxidoreductase, EC 1.11.1.7). Kinetic studies showed that cyanide ion fulfills criteria for a substrate for the peroxidase catalyzed reaction in the erythrocyte. From the behavior of the system, these authors suggested that the oxidation of thiocyanate in erythrocytes was catalyzed by an enzyme they named thiocyanate oxidase.

A search for an appropriate enzyme in erythrocytes was therefore made but none was found. Instead, the formation of sulfate and cyanide from thiocyanate in the erythrocyte was shown to be entirely accounted for by the peroxidase activity of hemoglobin (donor: H$_2$O$_2$, oxidoreductase, EC 1.11.1.7), as reported below.

EXPERIMENTAL PROCEDURE

Materials

KCN. $\text{Na}_2\text{SO}_4$ was prepared according to the method of Wood, Williams, and Kingland (2). $\text{Na}_2\text{SO}_4$ was prepared as described by Limonan (9). $\text{Na}_2\text{SO}_4$ and $\text{Na}_2\text{HPO}_4$ was purchased from American AnalaR. Aminothiol (3-amino-1,2,4-triazole) was obtained from Eastman Organic Chemicals. Horseradish peroxidase and catalase were obtained from Worthington Biochemical Corporation. Glutathione peroxidase was prepared from bovine liver. The method of Mills (9) was used in obtaining horseradish peroxidase. Reduced glutathione was prepared from raw skin milk as described by Morris and Haltiwanger (11). A hydrogen peroxide solution, 20 ml, was prepared immediately before use by dilution of a stock solution which was standardized every other week by titration with 0.1 N sodium thiosulfate. Bovine blood was obtained fresh from the packing house for these studies.

Hemoglobin—An hemolysate containing approximately 2.5 g of hemoglobin in 20 ml, which had previously been dialyzed against the buffering buffer, was passed through a column (8 X 62 cm) of Sephadex G-100 equilibrated with 0.1 M phosphate buffer, pH 7.4. The flow rate was 20 ml per hour with fractions of 10 ml per tube being collected at 6°. Appropriate fractions were pooled and concentrated by ultrafiltration. Further purification of the hemoglobin was carried out by the method of Hill and Davis (12) except that the buffer was not saturated with carbon monoxide. Conversion to methemoglobin was completed with potassium ferricyanide, and the excess ferricyanide was removed by dialyzing the solution exhaustively against 0.1 M sodium phosphate buffer, pH 7.4. The solution was then dispensed into small test tubes and stored in the deep freeze at -10° to be used within 6 months.

Oxyhemoglobin—The above procedure was followed except...