

BUCKWHEAT-POISONING

WITH REPORT OF A CASE IN MAN *

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Buckwheat-poisoning, or "fagopyrismus,"¹ may be defined as a disease which occurs in certain white or white-spotted animals that have been fed on the common buckwheat, *Fagopyrum esculentum* (*Polygonum fagopyrum*) or on the other species less frequently cultivated, *Fagopyrum persicaria*. Clinically, the milder forms of the disorder are associated with an itching erythema, situated mainly on the head and face, constipation and digestive disturbance, the more serious cases being attended by cutaneous, respiratory, febrile or urinary phenomena. Pathologically, there may be a vesicular, pustular, phlegmonous, or even gangrenous dermatitis, and inflammatory changes in the mucous membranes, the brain, nerves and lungs.

CAUSES

The etiology of fagopyrismus presents several features which deserve careful consideration. The disease is most common in swine and sheep, especially in pigs and lambs. It is occasionally seen in cattle and goats, and is rarest in the horse. White or spotted animals are said to be exclusively affected. Those that are black or artificially blackened escape the disease, and, curiously enough, the pigmented parts of the skin in diseased white-spotted animals remain normal.

The worst cases of buckwheat-poisoning are seen in animals that have been fed on the buckwheat plant while in bloom, but the malady may develop after the eating of the grains, bran, chaff, straw or stubble. In winter the disease manifests itself merely by burning and itching of

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1. Fagopyrismus is derived from the Latin *fagus*, beech; the Greek *pyros*, wheat, and the Latin suffix, *ismus*, a condition. Buckwheat is so named because of the resemblance in shape of its seeds to the triangular beech-nuts; hence the common name buckwheat and the botanical name "fagopyrum," both of which signify etymologically "beech-wheat." *Beech* and *buck* have the same root (cf. Ger. *buche*, beech; *buch*, buck—*buchweizen*, buckwheat; Anglo-Saxon *bok*, beech, buck; *bokwate*, beech-wheat, buckwheat). The buckwheat plant belongs to the order of *Polygonacea* (*polys*, many and *gony*, knee). *Fagopyrum esculentum* (edible buckwheat) is the species most widely cultivated.

the skin. Some years it is more prevalent and severe than others. Locality seems to bear a causal relation. Sunlight is an important contributing factor, it having been generally observed that animals fattened on buckwheat under shelter or cloudy skies acquire the malady very rarely, and then in the milder form.

The immediate cause is unknown. Dammann² asserts that fagopyrismus is primarily a local disorder of the unpigmented skin, due to the disturbing action of fungi that live on buckwheat, or that it is caused by the poisonous products of these parasites. In support of this theory, he points out the readiness with which the exposed parts of animals may become infected by actual contact with the food during the act of feeding. Schindelka² believes that the disease arises from the intestinal absorption of toxic substances which are generated in buckwheat either as a result of bacterial change, or because of peculiar telluric conditions. He argues that these bodies become active only under the chemical influence of the sun's rays, and provided there is no pigment lining to act as a barrier.

In view of the causative relation of sunlight to the development of buckwheat-poisoning, it is of importance to note the recent work of Hausmann,³ who, in a preliminary report on the "Sensitizing Action of Animal Pigments and Its Physiologic Significance," announces that bile possesses marked photodynamic power. He had previously shown that, under the influence of light, rapid hemolysis occurs when the extracts of chlorophyll plants are added to red corpuscles and that, on the other hand, no hemolytic action takes place if a similar mixture is kept in the dark. Experimenting with animal substances, he has found that prompt hemolysis results when bile is allowed to act on red cells in the presence of light. Control tests, in the absence of light, proved negative. Hematoporphyrin, he tells us, has even greater sensitizing properties, when activated by light, than bile itself. Hausmann also calls attention to the great resemblance of this photodynamic power of the extracts of chlorophyll plants to the photosynthetic assimilation processes of green plants as they occur in Nature. He also refers to the genetic relationship between hematoporphyrin and chlorophyll. In comparing their similarity, I have been struck with the fact that phyloporphyrin, a derivative of chlorophyll, not only closely resembles in structure the hematin derivatives, hematoporphyrin and mesoporphyrin, but that it

2. Hutyra and Marek: *Spezielle Pathologie und Therapie der Haustiere*, 1906, ii, 828.

3. Hausmann: *Die sensibilisierende Wirkung tierischer Farbstoffe und ihre physiologische Bedeutung*. *Wien. klin. Wchnschr.*, 1908, xxi, 1527.

shows almost the identical absorption spectrum which is characteristic of these two hematin derivatives. And, further, it is of great interest to note that when phytoporphyrin and hematin are submitted to reduction with concentrated hydriodic acid both yield hemopyrrol, and that hemopyrrol is converted into hydrobilirubin by the action of sunlight.

The accompanying diagram brings out more clearly these points of resemblance.⁴

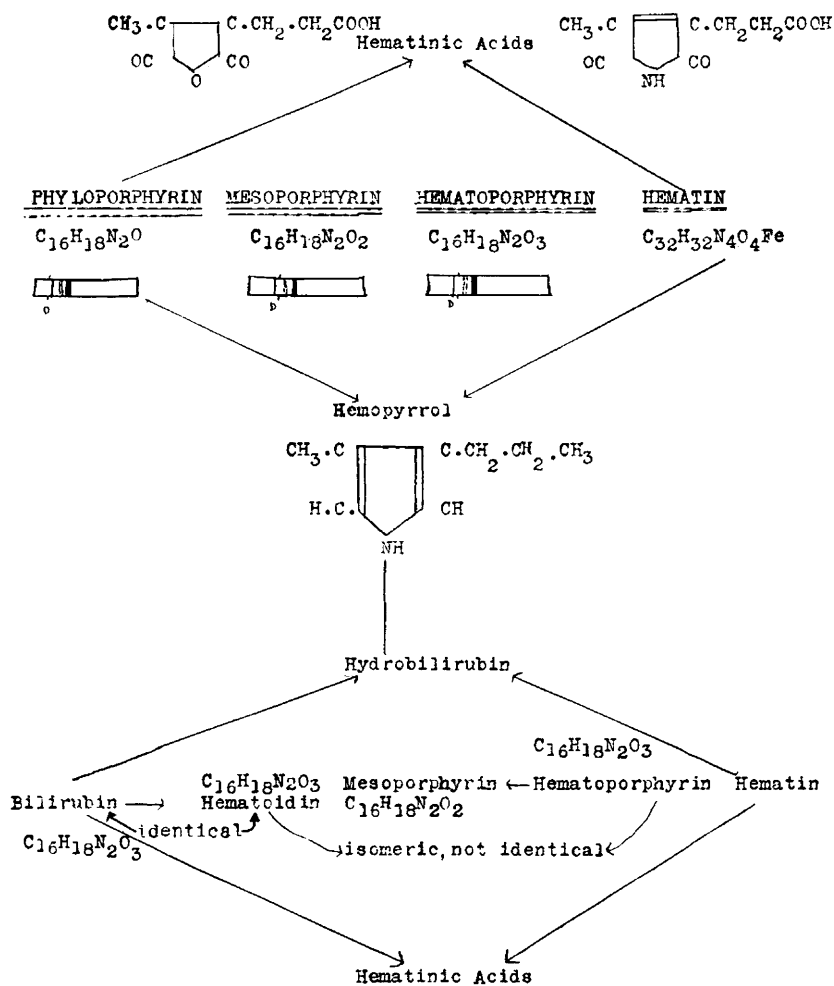
Hausmann³ is of the opinion that we have much to learn regarding the causative relation of the sensitizing coloring materials of our bodies to normal and abnormal processes. He suggests as not improbable the sensitizing action of bacterial products, and the possibility that certain skin diseases are caused either by an excess or insufficiency of the sensitizer. This theory gives the hint that fagopyrismus may be due to the photodynamic power of some substance which becomes a sensitizer by virtue of the specific action of the sun's rays, and that the transformation takes place while it is slowly passing through the peripheral blood streams of animals having little or no cutaneous pigment; and, further, it may be assumed that this substance remains inert and harmless in the bodies of the black animals, because of the failure of the sunlight to activate it through dense pigment.

SYMPTOMS

In the milder form of buckwheat-poisoning in animals an erythematous rash occurs which is situated on the head and face, especially on the ears and eyelids. It may extend to the throat or manifest itself in any unpigmented part of the skin. There is more or less swelling and intense itching. The erythema is followed by a brownish desquamation and later by more or less pigmentation. The severer cases occur during spring and summer. The eruption may be vesicular in type—the so-called sheep-pock. The vesicles vary in size from a lentil to large blebs, which on rupture exude a clear straw-colored fluid. Crust formation follows, and there is finally slight pigmentation. The skin is hot and swollen. The itching is apparently intolerable. The swelling may be so marked as to cause the eyelids to close and the ears to hang down. There are other cases which are characterized by a pustular or a phlegmonous dermatitis (the head-erysipelas of sheep) or even a gangrenous

4. Hematin, the prosthetic group of oxy-hemoglobin, is easily converted into hematoporphyrin, which latter shows a characteristic absorption spectrum. (The older and probably incorrect formulas are used, since they bring out the relations in a clearer manner.)

RELATIONS BETWEEN PHYLOPORPHYRIN AND HEMATIN
AND ITS DERIVATIVES.



By treatment of acet-hemin with hydriodic acid and phosphonium iodid, Nencki and Zaleski obtained mesoporphyrin, a substance having the composition represented by the formula C₁₆H₁₈N₂O₂ and giving an absorption spectrum closely resembling that of hematoporphyrin but somewhat nearer the violet end.

By treatment of chlorophyl with alkalies phyloporphyrin is obtained, which has a chemical composition represented by the formula C₁₆H₁₈N₂O and which shows the same characteristic absorption spectrum as the two hematin derivatives but still nearer the violet end of the spectrum.

By oxidation of either phyloporphyrin or hematin Kuster obtained two crystalline substances which he called hematinic acids and which were shown to be derivatives of pyrrol.

When submitted to reduction with concentrated hydriodic acid both phyloporphyrin and hematin yield hemopyrrol.

Hemopyrrol is converted into hydrobilirubin by the action of sunlight, and by suitable treatment both hematin and bilirubin can be made to yield the same substance.

The crystalline substance hematoidin, found in old blood clots, and surely derived from hematin, has been shown to be identical with bilirubin.

Like phyloporphyrin and hematin, bilirubin also yields the hematinic acids on oxidation.

form. Conjunctivitis, stomatitis, laryngitis and bronchitis more or less proportionate to the various skin lesions have been observed. The animals grow restless, wander aimlessly about and rub their bodies against hard objects. There are anorexia, retching, fever, dyspnea, cough, constipation, at times acute gastrointestinal disturbances and in some instances strangury. The group of cases showing marked disturbance of the nervous system may or may not be associated with skin lesions. Rabe⁵ reports epileptiform seizures in swine and horses without any skin disorder. Some of the animals become maniacal, cry out and jump and run about in a wild, excited manner. Again, others show signs of disturbance of the central nervous system by one or more of the following phenomena: rotatory movements, vertigo, severe cramps of the voluntary muscles, tremor of the extremities or lips. There may be the opposite picture of depression, stupor, coma or paralysis of the spastic or peripheral type.

Richter⁶ observed, in a number of swine that had been fattened on buckwheat, anorexia, dry stools, strangury, fever and dyspnea. In those that died there were found at autopsy inflammation of the mucous membrane of the stomach, inflammatory changes in the neck of the bladder (in one instance rupture of the viscus) and hyperemia of the lungs and brain.

Fagopyrismus may prove rapidly fatal in the cerebral form, or where there is urgent dyspnea due to the edematous narrowing of the air passages. Under proper management the symptoms usually subside promptly, but tend to recur after ten days or an even longer period if the animals are subjected to the blazing sunshine.

The treatment consists of immediate withdrawal of buckwheat as food, shelter from the sun, purgation, and locally the application of bandages saturated with cooling antipruritic lotions.

BUCKWHEAT-POISONING IN MAN

I have been unable to find any medical record of buckwheat-poisoning in man, except for the general statement in Gould's Medical Dictionary (see "buckwheat") that the free use of buckwheat tends to constipation, indigestion, headache and a peculiar roughness and itching of the skin. In 1897 von Jaksch⁷ quoted Kobert as his authority for the

5. Friedeberger and Fröhner's *Veterinary Pathology*. Translation by Hayes, 1908, i, 458.

6. Fröhner: *Lehrbuch der Toxicologie für Thierärzte*, 1890, p. 213.

7. Von Jaksch: *Die Vergiftungen*. Nothnagel's *Spezielle Pathologie und Therapie*, 1897, 548. Also Kobert: *Lehrbuch der Intoxicationen*, Stuttgart, 1893, p. 443. For literature, *ibidem*, edition 2, 1906, ii, second half, p. 585.

statement that no case of buckwheat-poisoning had been reported in man. Poisoning has been observed in the human being from eating the common beechnut. The symptoms were vomiting, headache, dyspnea, spasms of the larynx, similar to those seen in hydrophobia, and unconsciousness.

Rakun⁸ reported, in Petersburg, Russia, in 1899, two cases of poisoning, in a woman and her son, who developed restlessness, weakness, rapid pulse, dilated pupils, thirst, dryness of the throat and nausea, shortly after eating heartily of buckwheat gruel. The buckwheat in question had been bought at a neighboring grocery store—only just enough of it for the one meal. Rakun, however, went to the store, and, on examining that particular buckwheat there, found that it contained large quantities of henbane grains. He at once attributed the poisoning to the henbane and not to the buckwheat.

HISTORY OF AUTHOR'S CASE

The case of fagopyrismus which I have the privilege of reporting is that of a man who throughout his life has had a most remarkable hyper-susceptibility to buckwheat. He has gray eyes and a fair skin. His history, which he has been good enough to give me in detail, is of sufficient importance, I think, to report in full, practically in his own words. He says:

My first acquaintance with buckwheat dates back to 1863, when, at the age of 9 years, I was taken by the district school teachers to participate in a spelling contest. About 10 o'clock in the evening I ate heartily of a supper which was prepared at a near-by farm house. Buckwheat cakes were served at the end of the meal. When I had eaten a small part of a cake I began to experience great discomfort in my throat, gullet and stomach—I felt as if I had swallowed hot lead. I at once attributed it to the piece of buckwheat cake because of its strong and strange taste to me, having never before eaten of the food. I could not swallow another mouthful of the cake, nor endure the retching caused by what I had already eaten. I was obliged to leave the table for the open air. One of the company followed me out and advised me to seek relief by running my finger down my throat. The effort it cost me to dislodge the offending morsel served further to distort my features, which had already become grotesque. My eyes were blood-shot, my face was red and swollen, and my lips were knotty with large hives.

Somewhat frightened by my condition and by the disquieting remarks my appearance called forth, I decided to go home. I lived on a frontier farm three miles distant. The night was very cold, but I found the zero temperature soothing to my hot and itching skin, and the long walk in the snow helped me to regain my composure.

On reaching home my mother questioned me closely. She attributed my condition to violent exercise rather than to something I had eaten, as there had been

8. Rakun: *Otravleni grechnevoi Krupoi*. *Feldscher*, St. Petersburg, 1899, ix, 141. A translation of Rakun's report was kindly obtained for me by Major Walter D. McCaw, Librarian, Surgeon General's Office, Washington, D. C.

an intermission of twenty minutes allowed the boys for exercise, and I had been particularly active, joining them in wrestling matches and in other strenuous games. I stoutly maintained that the piece of buckwheat cake had caused all of my suffering. The following morning I had fully recovered from all traces of my unpleasant experience.

For years afterward I occasionally had attacks similar in nature but milder in form. Each time my mother had made cakes, mush or hot bread from a particular grist of corn-meal. Inquiry at the mill developed the fact that the corn was ground on the same set of stones which had been used for grinding the grains of buckwheat.

When traveling I am always on my guard against being served buckwheat cakes, declining invariably cakes of any kind when buckwheat cakes are on the menu, for no matter how carefully the batter of wheaten or corn cakes is made, if the cakes are cooked on a griddle that has been previously used for cooking buckwheat cakes I can not eat them and retain them.

Twice I have been served with buckwheat cakes when other cakes were ordered, and each time I have suffered desperately, although but one mouthful was swallowed. On the last occasion I managed to reach a doctor, but, before starting for his office, I drank a bowlful of mustard water, and on my way stopped at a drug store where I was given two teaspoonfuls of the wine of ipecac. When I reached the doctor he was visibly startled by my appearance. He gave me two doses of hive sirup, but it was fully thirty minutes before the desired effect was obtained. This was the longest time I have suffered before vomiting occurred. The burning exceeded anything I had previously endured. My face, eyes, tongue, neck, shoulders and hands were hot, inflamed and swollen, and my lips were thick with hives. The itching about my neck, shoulders and chest was unbearable; my lungs felt as if they had so tightened up that I could hardly get my breath; I coughed incessantly; the saliva dripped from my mouth and I rolled about on the doctor's floor in agony. Almost immediately following the action of the emetic I began to shake like one in an ague fit—the reaction, I suppose. This attack happened on one New Year's morning, and to give you an idea of the rapidity of my recovery, I made several social calls in the afternoon. I may add that for several days following my worst attacks, the skin of my hands, scalp and face sheds in little pieces.

For a number of years I thought I had the same idiosyncrasy for black pepper and certain ground spices, having had the same distress after eating highly seasoned foods, as soups, turkey dressing and the like. To settle this point I bought pepper berries and had them ground at my home. No trouble followed their generous use. Suspecting some form of buckwheat to be the adulterant in the ground spices, I once asked an agent of a large spice mill if such was the case. After some hesitation he admitted that his firm bought buckwheat hulls by the carload and had them roasted, ground and mixed with spices, particularly with black pepper. I have met with this adulteration in pepper but rarely in recent years.

My salivary glands are so susceptible to the buckwheat poison that I can readily detect buckwheat adulteration in food by simply holding a portion of the suspected morsel under my tongue. If there is buckwheat adulteration my tongue swells and burns and there is prompt increase in the flow of saliva, and, it is needless to add, that since I have known the usefulness of this precaution no particle of food has been swallowed that showed the presence of buckwheat contamination.

Once I was made very sick by eating honey which I noticed was rather dark. On tracing up its source I learned that it was made by bees that were allowed to feed on the buckwheat blossoms, and that this particular kind of honey was known commercially as "buckwheat honey."

I am seized with long-continued sneezing attacks if exposed for a moment to buckwheat meal that has been scattered about in the dry state. I have frequently had such annoyance to follow brief visits to grocery stores where buckwheat meal had recently been handled. Just lately I had a severe attack of sneezing. It began as soon as I reached my office. I at once asked if any buckwheat was in the room. My clerk seemed surprised and said, "Yes, there is a bag of it over there in the corner." It had been sent to me, without my knowledge, by an acquaintance of mine who knew nothing of my unenviable idiosyncrasy.

All nuts, except almonds and Brazil-nuts, affect me in a manner somewhat similar to buckwheat, except that the salivary glands are not nearly so sensitive, nor is the effect on the lining of the stomach so immediate or severe. The tightening up of the lungs and bronchial tubes is, however, more marked than in the case of buckwheat poisoning, the symptoms being not unlike asthma in extreme cases.

EXPERIMENTS

At my request, the patient submitted to the three following experiments. I had thought of testing the sensibility of his conjunctiva by instilling into the eye a few drops of a weak infusion of buckwheat, but at the suggestion of Dr. William S. Thayer the skin test was substituted. The experiment was made by Dr. Rufus I. Cole in Dr. Thayer's office, about 10 o'clock on the morning of the 26th of last November.

The left arm was scarified in two places under strict antiseptic precautions. Without the patient's knowledge, an amount containing a grain of buckwheat was taken from a sterilized infusion of the cereal and rubbed into the upper scarification, while a mixture of sterile flour and water was applied to the lower one. The denuded areas were situated about three inches apart. As controls, Drs. Thayer, Cole and I underwent a like procedure with uniformly negative results.

Within fifteen minutes after the vaccination the patient remarked, "The buckwheat is beginning to work." He complained of a "tight feeling" in his chest, and of nausea in the "pit of the stomach." He began to cough at frequent intervals, and there was noted increase in the respiratory movements; asthmatic breath sounds; rapid pulse which soon became intermittent; suffusion of the conjunctivæ; an erythema, more pronounced on the face, neck, forearms, hands, chest and back than on the buttocks, abdomen and lower extremities; intense pruritus; slight swelling of the features, hands and fingers; giddiness, restlessness and unsteadiness in the gait. The pupils remained normal. There was no thirst. Because of the asthmatic symptoms, Dr. Thayer gave the patient 1/100 of a grain of nitroglycerin.

The dressings which had been applied to the arm were now removed, and it was found that only the upper scarification showed any local reaction. Here there was an urticarial wheal the size and shape of a half-dollar piece. About this time the heart's action became so irregular and labored that it was decided to prevent further absorption of the buckwheat by cleansing the vaccinated area. Notwithstanding the fact that 95 per cent. alcohol was used, the lower scarification became contaminated with the buckwheat washings from the upper one, resulting almost immediately in the formation of a round wheal about the size of a nickel. It was fully an hour and a half after the onset of symptoms before the patient was physically equal to leaving the office.

He was seen by me late in the afternoon. The wheals had subsided, but the skin surrounding the scarified points was distinctly blanched. An occasional drop in the pulse, slight itching and a faint erythema on the face and hands persisted. The conjunctivæ had cleared up; fever and urinary symptoms were absent. No scar followed the vaccination.

On the afternoon of December 30, Dr. Cole made a control experiment in his laboratory at the Johns Hopkins Hospital. The arm was again scarified in two places and applications were made. The patient submitted to this second test after being assured that he would be promptly relieved at the appearance of the first symptom by immediate washing of his arm. No local or general disturbance resulted. The pulse was taken by me at frequent intervals and was found to be rhythmic and normal throughout. As a matter of fact, unknown both to the patient and myself, sterile water only had been applied to the scarified areas. It was a little disappointing, however, that the patient failed to sneeze, though seated near a bench on which a small amount of buckwheat meal had been scattered.

The third experiment was performed by Dr. Cole in his laboratory on January 27, 1909. The object of this test was to determine the patient's sensitiveness to buckwheat by mouth. The buckwheat used was obtained by me at a grocery store where it was advertised as the "dark, old-fashioned kind." It was decided to give the patient in succession unknown powders, some of which contained buckwheat, and to observe whether or not any marked reaction followed the administration of the buckwheat-containing powders. For each test an amount of powder about equal to that which could be held on the end of a knife-blade was placed on the patient's tongue and allowed to remain there for from five to ten minutes when he was directed to spit it out and to rinse his mouth thoroughly before the next powder was given. A separate wooden spatula was used for each test, and care was taken to prevent any trace of buckwheat gaining admission to the powders not intended to contain it.

Mixtures of the following substances were made and sterilized in test-tubes, the ingredients of which were indicated by suitable letters on the labels as indicated in the following key:

C. = Cornmeal.
 F. = Flour.
 M. = Maltose.
 G. = Glucose.
 B. = Buckwheat.

Test 1.—The powder contained G., F., M. and B. The patient did not detect the buckwheat and said that he felt sure the powder contained none.

Test 2.—The powder contained G., M. and B. There was no marked reaction, but the patient had a sensation of warmth in his mouth. He suspected buckwheat, and said that he felt confident that vomiting would result if he swallowed the powder. There was beginning suffusions of the scleræ and slight redness and itching of the face and hands.

Test 3.—The powder contained C., M. and F. No increase in the symptoms was noted. The patient said that he thought the powder contained no buckwheat.

Test 4.—The powder contained F., M. and G. Patient coughed a little, and complained of a little burning in his mouth, but did not regard the test as positive. There was a little increased redness of the face. He complained of itching in his mouth.

Test 5.—Same as 2, which patient considered suggestive.

Test 6.—A very small amount of pure sterilized buckwheat was placed on the tongue. The patient considered this test free of buckwheat.

Test 7.—A larger amount of the same pure buckwheat was given. The patient complained of burning in his mouth, and said he felt as though he had had a very slight trace of buckwheat.

Test 8.—Same as 2. No increase in symptoms.

Test 9.—Same as 7. No definite reaction.

It was now thought that the buckwheat being used was not active. We decided, therefore, to substitute some of the sterilized buckwheat which had been used previously in the test by insertion into the scarified area on the patient's arm on November 26.

Test 10.—This buckwheat, equal in amount to that of any of the powders employed in the foregoing tests, was placed on the patient's tongue. No violent reaction followed. The patient was doubtful at first if this powder contained buckwheat, but later he expressed himself as confident of its positive nature. He felt like vomiting and said that he must sit down. There was increase in his cough and hoarseness developed. Suffusion of face and scleræ became more marked. He complained of itching and burning in his mouth, and there was some drooling; the buccal and pharyngeal membrane became intensely red. The erythema was particularly marked and persistent on the chin. There were also redness and intense itching of the hands and fingers. On the lower lip near the right angle of the mouth two typical wheals developed. The pulse, which had been regular, increased in rate of 100 and then became irregular, dropping a beat in every eight or ten beats. I accompanied the patient to his office. He complained of tightness in his throat and chest, also of heat and itching all over his body. The drooling and dysphonia became more marked, and by the time he reached his destination he could barely speak above a whisper. I saw him again in half an hour's time, and found him somewhat better, but it was several hours before the symptoms disappeared.

The subject of fagopyrismus opens up an inviting field for further investigation. I shall report later the result of a series of experiments I am about to begin on animals.

In conclusion, I desire to thank Drs. Thayer and Cole for the interest they have shown in the case and for their valuable and generous aid.

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